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SURGERY OF THE HIP-JOINT*

PRESENT AND FUTURE DEVELOPMENTS

BY

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In the conditions of the modern world patients with osteoarthritis of the hip are inclined to consider surgical treatment for degrees of discomfort which less than twenty years ago were regarded as inevitable. The orthopaedic surgeon is presented with a problem which has changed completely in two decades. The methods of classical surgery in the past were able to produce gratifying results in osteoarthritis of the hip in patients with pain and fixed deformity, but to-day patients commonly present with hip disorder in such an early form that even the assistance of a stick is not required. A surgeon accepts great responsibility if he recommends surgery before a patient needs a stick, and it takes much soul-searching to decide whether the results obtained in early cases are commensurate with the time and money involved in treatment. The possibility of complications after major surgery in patients affected systemically by degenerative disease needs special consideration.

In a specialty as vast as that of orthopaedics, surgeons yearn for an easy hip operation, or if a good operation is difficult they hope that having mastered its performance through trial and tribulation it should be universally applicable. The orthopaedic surgeon is perturbed by the failure of the Judet arthroplasty, which had been accepted with open arms as respite from the

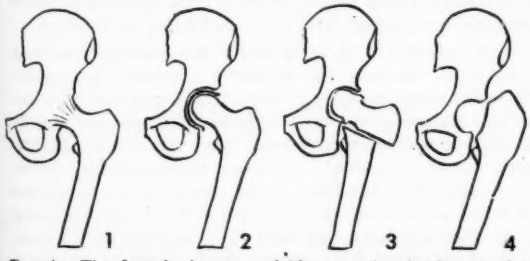

FIG. 1.—The four basic types of hip operation in degenerative arthritis. (1) Arthrodesis: sacrifice of mobility in the interests of stability and freedom from pain. (2) Arthroplasty: the attempt to preserve stability and at the same time retain mobility. (3) Osteotomy. (4) Pseudarthrosis: sacrifice of stability in an endeavour to guarantee mobility.

difficult and capricious operation of cup arthroplasty. The only type of operation that ever could be universal would be an arthroplasty, because this is the reconstruction of a normal joint, whereas operations such as arthrodesis will always be limited to special conditions.

Until an "all-purpose" arthroplasty is discovered the surgeon must select an operative method for each patient from one of the four basic procedures of arthroplasty, arthrodesis, osteotomy, and pseudarthrosis (Fig. 1), each of which has numerous technical modifications. How difficult this choice can be, and how it demands clinical experience and acumen, can be realized if we enumerate the factors that influence this choice. We can distinguish seven main groups of disorders of the hip-joint, each of which can be suitable for any of the four methods at some time in their evolution. Excluding tuberculosis, there are: (1) osteoarthritis, (2) rheumatoid arthritis, (3) old congenital subluxation and dislocation, (4) ankylosing spondylitis, (5) late complications of fracture of the neck of the femur, (6) miscellaneous infective conditions of the hip-joint, and (7) the salvage of unsuccessful hip operations.

The permutations and combinations of four operations and seven conditions are increased by four additional considerations: (1) what is suitable in middle-age may be unsuitable in later life; (2) what is suitable for unilateral hip disease may be unsuitable for bilateral; (3) what is suitable for an arthritic hip with a good range of movement may be unsuitable for painful ankylosis in bad position; and (4) what is best for a labourer may be unsuitable for a sedentary worker.

A successful arthroplasty would eliminate the intellectual task of choosing the best operation for the individual problem, but until this happy day arrives it is obvious that the surgery of the hip, far from being a small sub-specialty, is the beginning of a large subject. This type of surgery demands training in mechanical techniques which, though elementary in practical engineering, are as yet unknown in the training of a surgeon. Nowhere in the locomotor system would a liaison with university departments of engineering and colleges of technology be more rewarding than in the biomechanics of the hip-joint. For this reason, one of my aims is to indicate the need for establishing surgical centres to concentrate on the study of the reconstructive surgery of the hip-joint; in these centres men could be trained to master a repertory of different techniques and abandon the tendency, so common in the past, to be a "one-operation man." In such a centre it would be possible to acquire concentrated experience of numerous techniques and to decide the spheres of usefulness of different operations, both old and new.

Limitations of Arthroplasty

It is important to realize that factors exist which will for ever limit the scope of arthroplasty of the hip, no matter how we may study and improve the biomechanical design. It is all too easy to consider the reconstructive surgery of the hip as an exercise in engineering based

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on the mechanical distortion of the bones as revealed in the radiograph; but the bony changes are only part of the process which affects the soft parts and which produces the thick capsule and the weakened muscles. In hip disease a fixed adduction deformity indicates that the abductor muscles are defective; therefore to restore normal mechanical conditions in the joint will leave the arthroplasty to be motivated by weak abductor muscles, and adduction deformity and defective function may return. If the head of the femur is replaced by a polished sphere of stainless steel or plastic, surely it is a vain hope to expect an elderly patient to balance securely on the summit of this slippery "universal joint" if strong muscles do not exist to pull the body into balance. It is an axiom in hip-joint surgery that mobility and stability are incompatible, and it would seem reasonable to expect that the most serviceable result ought to be a compromise between these extremes.

That the soft tissues are abnormal in arthritic conditions of the hip can be demonstrated during the operation of "central dislocation" if an attempt is made to increase the exposure by applying manual traction direct to the head of the femur; it is possible to avulse the head of the femur from the side of the pelvis with comparatively little effort in some cases of arthritis, the capsule and even the psoas tendon peeling off the femur to expose bare bone with the greatest ease. But in osteoarthritis superimposed on congenital subluxation of the hip, which is purely a mechanical condition where we can expect the tissues to be healthy, this tearing procedure is quite impossible and every inch of exposure has to be obtained by sharp dissection.

Though these are the factors which limit the quality of an arthroplasty, this must not be taken as an absolute condemnation of arthroplasty, because there exist many patients in whom valuable amelioration has been obtained even though the results fall far short of perfection. But because this pessimistic aspect of the problem has been ignored only too often, patients have been led to believe that the results would be better than in fact they were. It is simply not true to say that the result of an arthroplasty depends on how hard the patient works at rehabilitation: no matter how well a patient co-operates, the quality of the final result depends on the quality of the tissues and on the sound mechanical design of the procedure.

Arthrodesis of the Hip

When hip disease is strictly unilateral the functional result of arthrodesis can be so good that it has to be seen to be believed. Whereas it is obvious that in bilateral hip disease some form of arthroplasty is essential, a considerable experience of operations deliberately designed to restrict the range of motion in the hip leads me more and more to believe that the indications for arthroplasty in *unilateral* hip disease are very few. The average result of arthroplasty leaves a patient in the same condition as the early stages of untreated osteoarthritis of the hip: the patient is a mild invalid with an uncertain future, is dependent on a stick, exercise tolerance is limited, and the hip causes a variable and unpredictable amount of mild discomfort. If originally the patient was severely disabled, an amelioration by arthroplasty to this extent will be gratefully appreciated. The result of an arthrodesis, on the other hand, if the opposite hip is normal, is in quite a different category: the patient is in no way an invalid; his condition is that of a person who has completely recovered from a disease but is left with a residual inconvenience.

The whole-hearted and unreserved gratitude of patients who have been totally relieved of pain as a result of arthrodesis of the hip is so striking that it forces one to realize that pain is the symptom which above all others must be cured in arthritis of the hip, and that the least significant complaint is "stiffness." There is here an interesting point in semantics: patients frequently complain of stiffness when the hip possesses a good range of movement; they often describe the discomfort of the hip as "it feels stiff." Some patients will be horrified by the proposition to stiffen the hip, because they do not appreciate how little they will notice the loss of motion after arthrodesis. With a stiff hip patients imagine that it will be impossible to raise the knee from the surface of the bed when lying supine; they are amazed to learn that it will be possible to lift the knee 6 to 8 in. (15 to 20 cm.) from the surface of the bed, which corresponds with a range of flexion at the hip of 20 to 30 degrees. Many patients with only a few degrees of motion in a painful hip will decline to have the hip stiffened, yet after arthrodesis the hip will actually feel looser; this is because a person with a painless arthrodesis is able to force the hip into postures which previously he was unable to tolerate when the hip was sensitive to passive straining.

In selecting patients for hip surgery it is obviously necessary to consider temperament and personality, and valuable light can be thrown on the magnitude of a patient's suffering by the response to the suggestion of arthrodesis. Anyone with unilateral osteoarthritis of the hip who will utterly reject the idea of arthrodesis without first giving it serious consideration is probably not ill enough for surgery and in all probability will be a difficult patient after arthroplasty.

An argument often advanced in favour of arthroplasty is that with a mobile hip the patient can reach the foot to put on shoes and stockings, cut toenails, etc. This is a most misleading idea, because many patients with early arthritis and a good range of flexion cannot even do these small offices before operation. Most patients after arthroplasty reach their foot by a trick movement from the side, and similar tricks are used after arthrodesis.

The operation of arthrodesis has acquired a bad reputation because by standard methods the post-operative convalescence is long, is often punctuated by serious complications such as thrombosis, and sometimes second operative interventions may be needed before bony fusion is secured. To cause permanent limitation of movement in the knee in the course of an operation undertaken to arthrodese the hip is a serious handicap to an elderly patient. For these reasons it has been sound clinical judgment for surgeons deliberately to choose a "second-class" arthroplasty rather than to try for a "first-class" arthrodesis by the only methods available in the past. I now believe that new ideas in arthrodesis of the hip will significantly shift the balance in choice between arthrodesis and arthroplasty.

Alternatives to Arthroplasty and Arthrodesis

There are conditions of the femoral head in osteoarthritis where cystic changes and bone sclerosis render the possibility of a bony fusion remote and therefore futile to consider. These cystic heads are often seen in the true malum coxae senilis. There is therefore a great need for a hip operation combining

the stability of an arthrodesis with a certain amount of mobility, and demanding only a short period of post-operative immobilization. A compromise to suit the problem of the elderly patient with monarticular osteo-arthritis of the hip would be one to function like an arthrodesis when walking, so enabling the patient to throw away his cane and strike the heel briskly on the ground without apprehension, while at the same time possessing a range of 20 to 30 degrees, which would make it possible to sit more perfectly than can an elderly patient with an arthrodesis.

Two operations are available which satisfy these requirements: displacement osteotomy and central dislocation stabilization.

Displacement Osteotomy

The idea of using a high osteotomy as elective treatment for osteoarthritis of the hip appears to have occurred almost simultaneously in England to McMurray and to Malkin, and it would appear that both these operators practised this operation with no attempt at a logical explanation of the successful results. Whereas a high osteotomy is a logical procedure when under-taken to correct fixed deformity, the same operation in a mobile hip seems irrational. It was suggested that the medial displacement of the distal fragment was an important element in the operation because this was supposed to impinge against the side wall of the pelvis to form a sort of by-pass to short-circuit the weight-bearing of the body away from the hip-joint.

Osteotomy is still a reliable method of abolishing pain in an osteoarthritic hip. There exists, however, the disadvantage that if plaster fixation is used in elderly patients there may be considerable trouble in recovering movement in the knee, and it may be nearly a year before a patient benefits from what has been a long and arduous experience. The potential for relieving pain by osteotomy has attracted the attention of numerous innovators, and new methods of internal fixation are being developed with the idea of enabling the osteotomy to be performed without plaster fixation. Experience with osteotomy has suggested that the mechanical explanation of relief of pain by medial displacement does not fit the facts, that relief of pain can be obtained by osteotomy without displacement of the femoral head, and that the mechanical problem is subsidiary.

This new attitude to osteoarthritis of the hip is of great interest and may lead to a completely new approach to the treatment of pain as a vascular problem in the femoral head. At the same time I remain decidedly sceptical on the results of an operation judged largely on the subjective element of pain, and, while keeping an open mind on this important aspect of the problem, my approach is primarily concerned with improving the mechanical stability and load-bearing capacity of the joint.

Central Dislocation Stabilization

This is an operation which I have been slowly evolving during the last eleven years. It has an advantage over the classical McMurray operation in that the post-operative recovery is quicker and less arduous for the patient. The load-bearing capacity of the hip is increased as indicated diagrammatically in Fig. 2. For maximum stability and comfort it is not desirable that more than 30 degrees of flexion should be obtained. This range of movement is adequate to ensure natural sitting while at the same time the patient can walk with a hip which is as stable as an arthrodesis.

In this operation the head of the femur is shaped into a cylinder, and the floor of the acetabulum is pierced by a hole large enough to receive the cylindrical head of the femur. This passage of the head of the femur through the floor of the acetabulum (Fig. 3) causes the

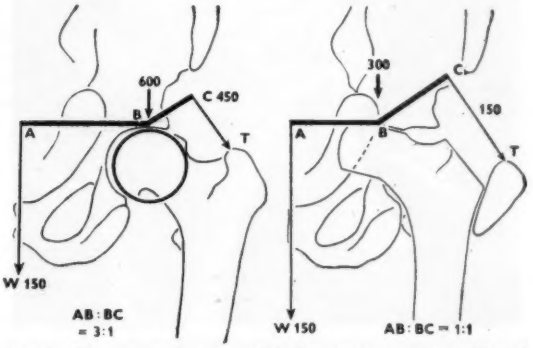

FIG. 2.—The mechanics responsible for the improved stability of the hip after central dislocation. In the normal hip the weight of the body acts as a lever nearly three times longer than do the abductor muscles. After central dislocation, with reattachment of the great trochanter laterally, the mechanical advantage of the gluteal lever is increased and the leverage of body weight is reduced.

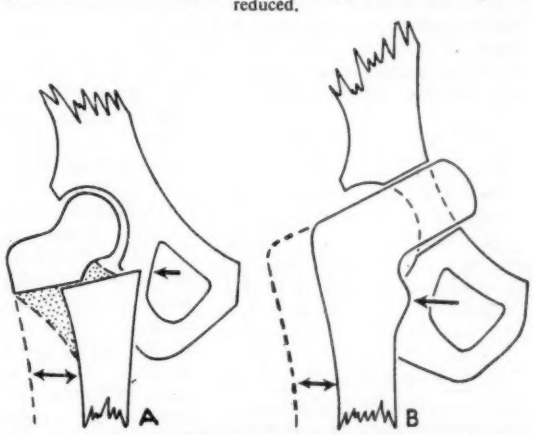

FIG. 3.—The central dislocation procedure (B), showing the basic similarity with the McMurray displacement osteotomy (A). Medial displacement of the line of weight-bearing is common to both procedures and is the mechanical explanation of improved stability.

base of the neck and the region of the trochanters to abut against the lips of the acetabulum and produce a bone-block between the femur and the pelvis. After this operation a minority of patients with osteoarthritis, perhaps 25%, eventually develop a spontaneous bony fusion, but the majority retain a fibrous ankylosis (Fig. 4). The remarkable feature is that this fibrous ankylosis is painless, and one presumes that this must be the result of being supported by the bone-block. The deliberate encouragement of a fibrous ankylosis of the hip is against all accepted canons of surgery, because, in the absence of a bone-block, a fibrous ankylosis of the hip is notorious for developing a progressive flexion-adduction deformity with defective function and return of pain. An experience of eleven years and about 250 cases has convinced me of the value of this procedure, and whatever defects there may be are offset by the short post-operative recovery and the preservation of full knee

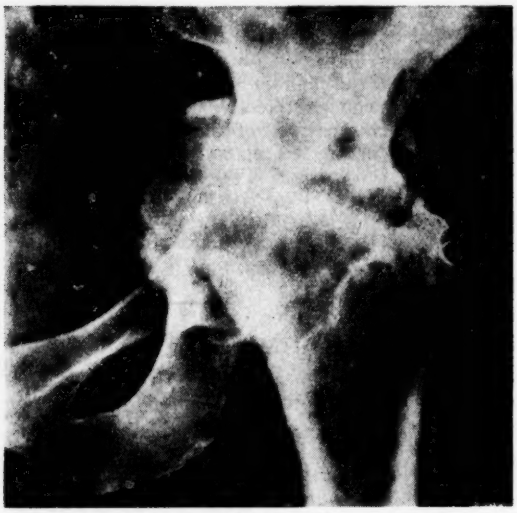

FIG. 4.—Typical fibrous ankylosis accompanying the central dislocation operation.

movement, which makes it available as a method of relieving pain in elderly patients.

The role of the bone-block in restricting rotation and flexion cannot be questioned, but the role of the bone-block in resisting adduction needs special comment. From late results it now seems clear that relief of pain and effective weight-transmission are often obtained without a block to adduction. This agrees with observations on the McMurray displacement osteotomy (M. M. Shepherd and G. V. Osborne, personal communications). Contrary to my original opinions, it now seems probable that to strive for a rigid bone-block to adduction at the time of the operation is something to be avoided, because it may expose the neck of the femur to such a rigid mechanical couple when bearing weight as to cause a fatigue fracture in 5 to 10% of these cases. To avoid the mechanism likely to fracture the neck of the femur I now strive to produce acceptance of weight by the femur as near to the base of the neck as possible, by shaping the femoral head into a varus position.

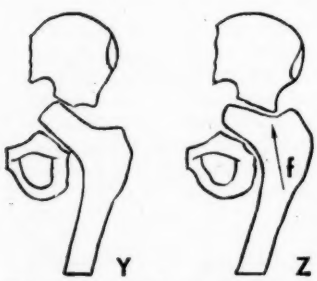

FIG. 5.—The simple central dislocation operation shown in its original form (Y). It can be seen that the neck of the femur is exposed to strong angulatory strains, which can cause it to fracture by fatigue. In the more recent development (Z) an attempt is made to achieve transmission of weight by "neck-bearing" of the acetabulum.

The operation causes some shortening of the leg; this is not usually more than three-quarters of an inch (2 cm.) of true shortening. It is important to mention this to the patient before the operation, because it is a good test of the patient's desire to be rid of pain if the idea of shortening is accepted with equanimity.

The hip is put into a single-sided hip spica with a little more abduction than is desired in the final result. The foot and ankle are left free to encourage venous return by the "calf pump." The hip spica is retained for six weeks, during which time the patient can get up and bear weight in the plaster as soon as the general condition permits. The last fortnight in plaster is devoted to early mobilization of the knee by cutting the hip spica down to free the knee-joint. The average period in hospital is eight weeks, and at the time of going home the patient is usually fit to look after herself without assistance.

A technical detail which I think is of value is reattachment of the great trochanter to the outer surface of the shaft of the femur at the conclusion of the operation. This improves the mechanical stability of the hip, reduces any tendency for a late adduction deformity, and assists in holding the femur in full central displacement.

Physiotherapy is not required, as a full range of movement in the knee is never lost and rehabilitation consists of nothing more complicated than encouragement in gentle walking. Most patients are fit for simple domestic duties three months after the operation.

In the minority of patients in whom a fatigue fracture has occurred the result has been salvaged by an osteotomy which, by removing the leverage of the length of the femur, causes union of the fracture and often produces a sound bony fusion of the whole hip.

Disappointing results which I have been shown by others endeavouring to use this technique have invariably been associated with the recovery of too much mobility in the hip, over 40 degrees of flexion range, as a consequence of failing to secure adequate penetration of the femoral head.

Arthrodesis by Central Dislocation

While there is no denying the excellent function of a good arthrodesis of the hip, the problem of obtaining osseous union in every case is difficult. If ever any patient is to cope with the inconvenience of a stiff hip it is of paramount importance that full range of movement should be preserved in the knee. The operation of central dislocation can be modified to procure an arthrodesis without significant prolongation of fixation which would prejudice mobility of the knee, and this technique has the safeguard that, even if osseous union were to fail, the result would still be functionally acceptable as fibrous ankylosis ("the second line of defence").

Experience is accumulating to suggest that often it is possible to predict whether a hip is likely to arthrodese, or become a fibrous ankylosis, from consideration of the age of the patient, the nature of the disease, and the radiological appearance of the bone. In cases where there is considerable cystic degeneration and sclerosis in the femoral head, the probability of a fibrous ankylosis is great no matter what steps are taken in the hope of bony fusion. On the other hand, patients below 45 years of age have a strong tendency to bony fusion because the conditions responsible for arthritis at this age (mild degrees of congenital subluxation, mild infective healed arthritis, and atypical varieties of osteoarthritis) are associated with a full blood-supply in the femoral head without sclerosis and cyst formation.

To adapt the central-dislocation procedure to obtain an arthrodesis the femoral head is made to fit accurately into the hole in the floor of the acetabulum by making it conical, so that it fits the hole like a cork in the neck of a bottle. A spring-loaded compression screw locks the bones together, reinforced by a block of cancellous

bone inserted between the dorsal lip of the acetabulum and the inner surface of the great trochanter (Fig. 6). A single-sided hip spica is applied and knee movements are begun by cutting away the back of the plaster below the knee after the first four weeks. Plaster is retained for a total of eight weeks and unrestricted weight-bearing permitted at eight weeks. The compression screw has spring-loading and the maintenance of pressure can be

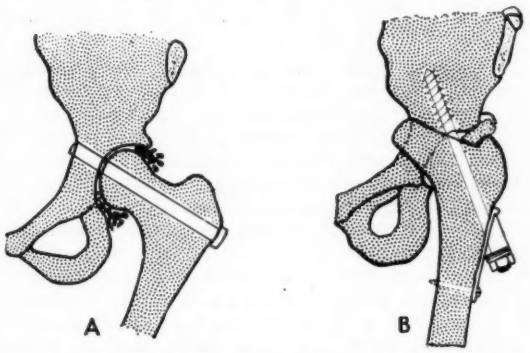

FIG. 6.—Arthrodesis of the hip by the central-dislocation method. In the orthodox procedure of hip arthrodesis (A) the strain on the nail is obviously very severe. In the central-dislocation procedure (B) the interlocking of the bones removes mechanical stress from the compression screw which is used as an adjuvant to fixation.

followed by weekly *x*-ray films during the first month; if it is thought imperative to obtain osseous union and there is evidence of compression being lost, as manifested by expansion of the compression spring, there are occasions when retightening may be considered.

Arthrodesis of the Hip in Difficult Problems

A special centre devoted to the surgery of the hip accumulates problems where an arthrodesis would be the desired solution but where the femoral head is missing or is affected by ischaemic necrosis. This type of patient often is young enough to tolerate three months of plaster fixation. Arthrodesis of these difficult cases has been successfully obtained from experience gained in the central-dislocation operation. The operation is performed in two stages separated by an interval of four to six weeks. If the femoral head is present, this

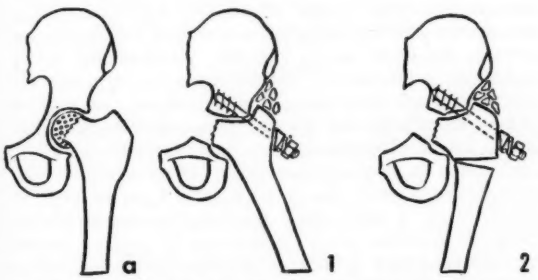

FIG. 7.—Arthrodesis of the hip in difficult problems. Ischaemic necrosis of the femoral head after a high subcapital fracture (a). First-stage arthrodesis (1) with central dislocation of stump of the femoral neck and approximation of the great trochanter to the dorsal lip of the acetabulum in abduction. Spring-loaded compression screw and bone-grafts applied above the great trochanter. Second-stage procedure (2) osteotomy and realignment of the limb in the functional position. The delayed osteotomy precipitates osseous union in the hip by removing the leverage of the length of the femur.

can be dislocated centrally, but otherwise the base of the neck is approximated to the lips of the acetabulum by means of a spring-loaded compression screw. Grafts of iliac chips are applied liberally between the great trochanter and the lateral wall of the pelvis (Fig. 7). At this first stage it may be necessary to place the hip in considerable abduction in order to approximate the living bone of the great trochanter to the living bone of the dorsal lip of the acetabulum and so avoid the difficult problem of grafting across a gap. At the second stage a high intertrochanteric osteotomy is performed to correct the excessive abduction and at the same time to remove the levering action of the long length of the shaft of the femur so that the "de-functioning" osteotomy precipitates osseous fusion in the hip-joint with a high degree of certainty.

Future Developments in Arthroplasty

Though we still lack a reliable arthroplasty, research to find one must continue even if its use is confined to the treatment of bilateral osteoarthritis and rheumatoid arthritis. Of all the elaborate operations which have been tried in attempts to reconstruct the conditions of the normal hip, the only one to have survived 25 years in the surgical repertory is the Smith-Petersen cup arthroplasty. Though much less frequently used than formerly, because its results are unpredictable, when they do occur the good results of the Smith-Petersen cup operation can indeed be exceedingly good. But it is difficult to decide if we have learned anything from this operation to help us with further developments because the results of cup arthroplasty do not correlate with mechanical or anatomical factors; as judged mechanically, unsuccessful results may have the cup in perfect position and successful results may have the cup in a poor position. The fact is that the mechanical design of the cup arthroplasty is not sound and Nature sometimes appears to realize this.

However, the cup operation has shown us that a good range of movement combined with reasonable stability cannot be obtained in hip arthroplasty unless an artificial structure is interposed between the head of the femur and the acetabulum. We have also learned the very valuable lesson that in certain conditions, which at the moment cannot be defined, raw bone can be made to generate new articular cartilage when in contact with a polished surface (the "mould" principle of Smith-Petersen). It is possible that the good results of cup arthroplasty depend on this fortuitous circumstance triumphing over the defective mechanical design of the cup arthroplasty.

The Judet operation, in which the femoral head is discarded and replaced by a prosthesis, has failed more completely than the Smith-Petersen cup, but, strangely enough, has probably taught us much more about arthroplasty. We have learned that in prosthetic replacement of the femoral head a close correlation exists between the functional result and a sound mechanical concept of the operation. The failure of the Judet is a *late* failure, due to mechanical failure of the bond between living bone and the prosthesis; but in the early stages, while the bond remains mechanically sound, the results, judged on the range of movement, the muscular control, and the freedom from pain, have had no equal and far outstrip the early results of the Smith-Petersen procedure, whose concept is totally unsound from a mechanical point of view. We can

therefore take encouragement that ideas based on sound biomechanical concepts may yet prevail.

One aspect of mechanical research into arthroplasty which has not previously received adequate attention concerns the frictional resistance to the motion of an artificial femoral head in the acetabulum. I have collected the evidence to show that the coefficient of friction of normal articular cartilage is phenomenally low (Charnley, 1959), and is in fact lower than anything encountered between solid substances in engineering practice. The coefficients of friction between bone and the substances commonly used in arthroplasty (stainless steel, chrome-cobalt alloy, and "perspex") are many times inferior to the coefficient of friction between normal articular cartilage. The only solid which has a coefficient of friction remotely approaching that of articular cartilage is the plastic polytetrafluorethylene (P.T.F.E.; "fluon"; "teflon"). This has a coefficient of friction better than that between steel and bone, but it still does not approach that of articular cartilage. Preliminary experiments with this substance—which has been under trial for three years—have shown very encouraging results, and, though the method is not yet suitable for general use, it points the way to further work.

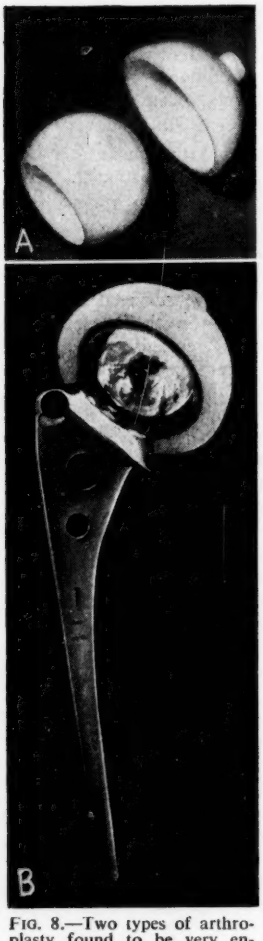

FIG. 8.—Two types of arthroplasty found to be very encouraging in rheumatoid arthritis. (A) Concentric shells of P.T.F.E. used to apply low-friction coverings to the articulation. (B) Stainless-steel prosthesis articulating with a P.T.F.E. socket.

The idea behind the use of a low-friction substance in arthroplasty is not merely in an endeavour to eliminate wear on the surface of the prosthesis, which in the Judet prosthesis is a sign of adverse frictional conditions. The low-friction concept would eliminate any twisting stresses being transmitted to the bond between prosthesis and living bone as a result of frictional resistance in the hip when walking. If a prosthesis could be devised which offered no frictional resistance to rotation in the acetabulum, the bond between prosthesis and femoral neck would be exposed to a force acting purely in a vertical direction and uncomplicated by twisting strains.

My initial experiments with P.T.F.E. used this substance as a "synthetic cartilage." The acetabulum was lined with a thin shell of the material, while the head of the femur was similarly covered with a hollow sphere (Fig. 8). It was hoped that motion would take place preferentially between the two slippery P.T.F.E. surfaces rather than between one of the P.T.F.E. surfaces and the bone to which it was attached. If the P.T.F.E. implant remained stationary in relation to the subjacent bone, there seemed some hope that mechanical bonding might improve if bone grew into irregularities provided for this purpose.

The difficulty with this design is the possibility of ischaemic necrosis of the remnant of femoral head included inside the cup.

It seems likely that a reliable and valuable amelioration of hip disability can be obtained by forms of arthroplasty developed from this idea, and especially in rheumatoid arthritis, where the prosthesis will never be exposed to very severe mechanical stresses because the patient's activity is invariably restricted by other joint lesions. It appears possible to guarantee the range of motion and freedom from pain after this operation, and a remarkable feature is the almost total absence of new bone formation with loss of motion which is so common in arthroplasty by other methods in rheumatoid arthritis. It is much too early to pronounce on the duration of symptomatic relief. It is probable that in future developments a prosthetic replacement of the femoral head, articulating with a P.T.F.E. socket, will prove more desirable than the double concentric shell of P.T.F.E.

Summary

The failure to discover a thoroughly reliable arthroplasty of the hip-joint renders it necessary to employ a number of operative techniques, both old and new, and to study the indications for each according to the clinical problem. When the contralateral hip-joint is normal, operations which abolish pain at the expense of movement probably give the most reliable results. A method of arthrodesis is described which I believe is free from the disadvantages which in the past have limited the use of arthrodesis in osteoarthritis. The possibility of abolishing pain and partially retaining motion by means of osteotomy is a field of investigation which is being intensively explored; it is possible that important biological information regarding the origin of pain in osteoarthritis may evolve from these surgical experiments, but it is too early to make any final opinion.

As regards arthroplasty, the only reliable method of obtaining a large range of motion while preserving reasonable stability demands anatomical reconstruction of the hip-joint, using metallic interposition or a prosthetic replacement. Experiments to improve the mechanical efficiency of arthroplasty, using new plastics having extremely low friction properties, suggest that in the future arthroplasty may have an ideal sphere of application in rheumatoid arthritis. Whereas in the past rheumatoid arthritis has been regarded as unsuited to arthroplasty, it now seems possible that the restricted demands required of an arthroplasty by patients whose activity is limited by disease in other joints may make it possible for them to benefit greatly by techniques which would not stand the wear and tear inflicted on them by less-disabled sufferers.

REFERENCE

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OPERATIVE TREATMENT OF OSTEOARTHRITIS OF THE HIP

BY

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At the end of the war the operative treatment of degenerative arthritis of the hip at this hospital was largely confined to three common procedures. Arthrodesis of the affected joint was regarded as the operation of choice in the younger group of patients, particularly when the condition was unilateral. Where mobility of the hip was required simple excision of the femoral head and neck, with the production of a pseudarthrosis as recommended by Girdlestone in 1938 (quoted by Batchelor, 1948), had a limited popularity. One of the major criticisms of this operation was the instability which followed, and the osteotomy practised by Batchelor (1948) appeared to have the advantage of additional stability, though probably requiring a rather longer period of convalescence. At this time the intertrochanteric osteotomy described by McMurray (1939) was not widely practised.

A new stimulus to the surgery of the hip was produced by the painstaking work of Smith-Petersen (1939, 1948) in the production of the mould arthroplasty. The operation that was finally devised appeared to have great advantages over the older methods of fascial arthroplasty, and revived interest in this country in the production of a stable, mobile, and painless joint. The shape of the Smith-Petersen vitallium cup was later modified by Adams (1953), who produced two models, the first in acrylic resin and the second in vitallium. One of the disadvantages of the Smith-Petersen arthroplasty was found to be the long period of rehabilitation demanded by the new hip-joint, and the more rapid results which Judet and Judet (1950) showed were seized upon with some enthusiasm. Unfortunately the early results of this operation were not maintained, and the use of a prosthesis of this type has largely been abandoned.

Many reviews of the results of hip surgery have been devoted to an assessment of the value of a single procedure. In this unit most of the common operations upon the osteoarthritic hip have been performed, and it appeared that a long-term survey of the results was due. With this in mind the present investigation was undertaken.

Material

During the ten-year period 1947 to 1956, 290 operations were performed in the orthopaedic unit at Guy's Hospital for degenerative arthritis of the hip. The types of operation are indicated in Table I.

TABLE I.—*Types of Operation Performed*

Type of Operation	No. Performed	No. Reviewed
Arthrodesis { Watson-Jones	90	54
Arthrodesis { Brittain	12	7
Cup arthroplasty	72	30
Replacement arthroplasty (Judet)	46	28
Girdlestone's pseudarthrosis	25	6
Batchelor's pseudarthrosis	20	13
McMurray's osteotomy	15	10
Other operations	10	6
Total	290	154

The number of patients subjected to operation was 239. Many of these required more than one operation upon the hip, and in some both hips were treated. The difficulties of tracing and persuading these patients, many of whom were very elderly, to come for review were great. Some had died during the intervening years, many lived too far away or were too old, and some had moved away and could not be found. Those who were examined formed just over half the total, and were probably a reasonably representative group. Of the rest, there were a large number who replied to a postal questionary, the results of which tend to confirm those obtained from personal examination, though they are not in fact included in this review.

Eight patients did not leave hospital after operation, and the cause of death in these was pulmonary embolism in four, massive collapse of lungs in one, cerebral haemorrhage in one, cardiac failure in one, and post-operative shock in one. Though this indicates a mortality ratio of almost 3%, there have been no deaths after operations upon the osteoarthritic hip during the past five years.

In comparing the results of various operations upon the hip it is important to consider what influenced the choice of surgical procedure. Table II is thus of interest,

TABLE II.—*Analysis of Type of Operation and Year*

	Arthrodesis	Cup Arthroplasty	Judet	Pseud-arthrosis	Other Operations
1947	3	1		1	1
1948	3	4		5	2
1949	4	10		7	
1950	7	10		6	2
1951	9	12	32	2	3
1952	11	11	14	3	2
1953	18	16		7	5
1954	20	7		9	2
1955	13	0		3	3
1956	14	1		2	5
Total	102	72	46	45	25

as it shows the popularity of operation year by year. Clearly, the condition of the patients coming for treatment has varied much less than the fashion for a particular surgical procedure. The patient who was suitable for a cup arthroplasty in 1948 was equally suitable for a replacement arthroplasty in 1952. Certain operations, however, have tended to be regarded as salvage procedures, and have been performed upon the more disabled patient, often as a secondary procedure. This type of selection must have some influence upon the result.

Method of Assessment

The two major symptoms of these patients are pain in the hip and limitation of physical activities. The latter is largely a function of pain, but fixed joint deformities also play a part. These symptoms were classified in the following way:

Pain.—0 = None at any time. 1 = Slight pain on activity. 2 = Considerable pain on activity, little at rest. 3 = Severe pain night and day, usually requiring analgesics.

Limitation of Activity.—0 = Full activity. 1 = Unessential activities avoided. 2 = All activities curtailed, difficulty in walking. 3 = Confined to the house.

From the pre-operative records, aided by the patient's own memory, an analysis of pain in the back and both hips, the limitation of activity, and the range of joint movement was compiled. For the post-operative assessment these features were supplemented by a record of the gait, the range of knee and spinal movements,

and a clinical estimation of the length of the legs. At the conclusion of the examination both hips were radiographed. The appraisal of the operations has been made largely upon the relief of pain, the restoration of activity, and, to a limited extent, the range of joint movements. The more detailed systems of assessment described by Gade (1947) and by Shepherd (1954a) have not been used, largely because of their complexity. It has been found that the following standard expresses in general terms what the surgeon and the patient feel about the results of an arthroplasty. (Clearly an arthrodesis must be assessed on a slightly different basis.) Good: complete relief of pain, with retention of a useful range of movement. Fair: result impaired by residual pain, stiffness of the hip, or instability. Poor: no relief.

The description of hip movements also needs some elaboration. The range of movements permitted often varies from day to day, and an accurate assessment is of little value. In using flexion of the hip as an index of mobility the most easily measured direction of movement has been taken. This is probably also the most important, though a small range of abduction is of great value. In very general terms the retention of other movements has been in proportion to the range of flexion remaining.

Arthrodesis

During the period under review 102 patients were subjected to arthrodesis of the hip. In those patients in whom degenerative changes followed tuberculosis of the hip in childhood Brittain's arthrodesis was performed. In some cases this was modified by using the fibula as a graft, immediately above the osteotomy site. These patients were immobilized in a plaster spica for 12 to 16 weeks.

When the degenerative changes were not infective in origin the arthrodesis was performed in the way which has been described by Watson-Jones and Robinson (1956). The hip was exposed by modified Smith-Petersen incision and the head of the femur dislocated. After removal of articular cartilage from the acetabulum and the head of the femur, the joint was transfixed by a long trifin nail. The arthrodesis was usually reinforced with a small graft cut from the ilium and slotted into the femoral head. Bone chips from the same source were placed around the joint. In the course of the operation only one major difficulty was noted—that of secure fixation of the two bones. In some cases the nail failed to penetrate the acetabulum adequately and the head of the femur sprang back, leaving a considerable gap between the two bones. This difficulty tended to arise in younger patients where the acetabulum was unduly dense, but in no case did it necessitate the abandoning of internal fixation. At the conclusion of the operation some patients were left lying free in bed, others had a short hip spica applied, but the majority were immobilized in a single hip spica for a period of about 10 weeks.

Results of Operation

As the object of these procedures was to secure bony ankylosis of the hip, the condition of this joint has been critically examined. The hip was considered to be arthrodesed when no movement could be detected at the joint and when the radiographs showed bony trabeculation passing from the femur to the ilium. The results are indicated in Table III.

TABLE III.—*Arthrodesis of the Hip*

		Total No. of Hips	Bony Ankylosis
Brittain & Watson-Jones	Following tuberculosis	5	5
	,, arthroplasty	2	0
		54	36

The number of patients subjected to ischio-femoral arthrodesis is too small to be of much significance. Two patients who failed to attend are known to have required further operations upon the hip, and presumably, therefore, bony fusion was not achieved. The two failures after arthroplasty confirm that arthrodesis as a secondary procedure is difficult and rarely successful.

As a result of the Watson-Jones procedure, only two-thirds of these patients secured bony fusion. Most of the rest had a short fibrous ankylosis in which movement was just detectable, but occasionally the range of movement was considerable. The rates of fusion after this type of arthrodesis have been variously reported. Thus Brown (1954), reviewing 31 hips from the same department treated surgically during the period 1942–6, found fusion in 27. Watson-Jones and Robinson (1956) in a personal series of 120 cases found all but seven had fused by bone. The surgical technique was similar, though the post-operative period of immobilization was longer and much stricter, and four patients required a second operation.

In reviewing the results of hip arthrodesis Stinchfield and Cavallaro (1950) found a pseudarthrosis rate of 23%, while Apley and Denham (1955) considered that fusion of the hip occurred in only 13 out of 20 patients in whom arthrodesis was attempted without osteotomy. These figures relate to the work of more than one surgeon, and the rate of fusion will always be found to be higher (as it is in the present series) with a single operator of wide experience.

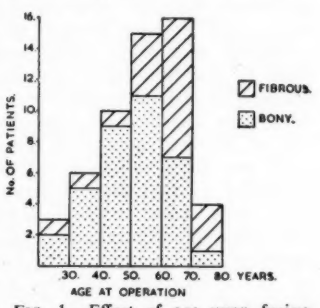

FIG. 1.—Effect of age upon fusion. Over the age of 60 the fusion rate in arthrodesis of the hip declines sharply.

In an attempt to discover the patients in whom pseudo-arthrosis was most common, the rate of fusion according to age has been considered, and is presented in Fig. 1. Up to the age of 50 only three hips of 19 failed to unite by bone. Above this age the fusion rate declined sharply, and over the age of 60, only 8 out of 20 hips showed a bony ankylosis. It is therefore suggested that the apparent deterioration in the rate of fusion, in this unit at least, lies in the increasing age of the patients who have been selected for this operation.

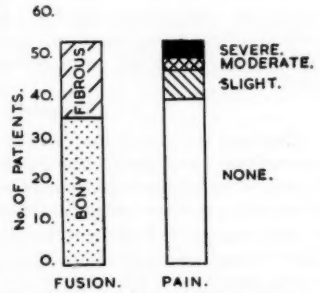

FIG. 2.—Results of hip arthrodesis. A bony fusion is associated with complete relief of pain; fibrous union may be painless, but more commonly gives rise to hip discomfort.

The object of arthrodesis is to relieve hip pain, and, as Fig. 2 shows, this was achieved in about three-quarters of the patients. The presence of a bony ankylosis was always associated with complete relief of hip pain, unless there was some reaction around the pin, which occasionally required removal. A short fibrous ankylosis was compatible with almost complete relief of pain, and indeed it is surprising how few of these patients admitted to more than an occasional discomfort in the hip. However, the pain in seven patients was considerable, and four of these required a further operation.

Assessment of function after the operation was complicated by the increasing age of the patient, and sometimes by the presence of degenerative changes in the other hip. However, most of the younger patients were able to engage in heavy work. In the more elderly the arthrodesis undoubtedly presented difficulties which are often ignored in the assessment of their disability. Though all were grateful for the relief of pain, some had difficulty in dressing, and many could not get up stairs. Some found it difficult to keep themselves clean at toilet. These difficulties appeared to be greater in patients with a relatively mobile hip pre-operatively than in those in whom the pre-operative range of movement was small.

Complications

Stiffness of the knee after immobilization in plaster was not seen during this series, and every patient had a range of movement of more than 90 degrees of flexion. On the other hand, degenerative changes in this joint were common, particularly when it had previously been the site of a long-standing osteoarthritis. To some extent this was influenced by the position of the arthrodesed hip. Any internal rotation deformity at the hip undoubtedly added to knee strain.

The optimum position of arthrodesis of the hip varied from patient to patient. Excessive internal rotation produced an unsightly gait. The neutral or mild external rotation position caused no disability, and external rotation had to be gross before it interfered with walking. Variations in the degree of abduction of the femur on the pelvis appeared of little importance, though the adducted position gave a slightly better gait. The greatest problems in walking were seen in patients with varying degrees of flexion deformity. It is notoriously difficult to assess the position of the hip on the operating-table, and this accounts for the wide range of positions which were seen. The gait was best in patients in whom the leg was fixed in the extended position, but for the older patients sitting was easier with a flexion deformity. When this exceeded 30 degrees, however, progression without a stick was impossible. For the most part excessive flexion was seen in patients with a failure of bony union, and a progressive flexion deformity even in the absence of pain was undoubtedly a severe disability.

Fracture of the femur at the level of insertion of the pin occurred in five patients. This was the most common, and the most serious, of the later complications. These fractures often occurred from trivial violence, but appear to unite readily. The incidence of fracture (10%) is higher than in most reported series; indeed, this is a complication which is frequently not mentioned.

One of the most encouraging features of this group is the response of the contralateral hip to arthrodesis. When the degenerative changes were initially unilateral they remained so. When the second hip was already deteriorating, a successful arthrodesis on one side usually enabled the patient to carry on without undue difficulty, and none of these patients subsequently required surgical treatment of the second hip. A study of the changes in the range of movement of the second hip, and of the radiographs, indicates that deterioration during the period of observation has only been slight.

It is now generally agreed that back pain after arthrodesis is not a significant problem provided the lumbar spine is relatively normal pre-operatively. The present review has confirmed this. Indeed, most of the patients with pre-operative back discomfort found that this was alleviated by arthrodesis of the hip.

McMurray's Osteotomy

Intertrochanteric osteotomy was performed upon 10 patients. In three of these the osteotomy was used to correct deformity of a hip which was already ankylosed, either by fibrous tissue or by bone. The seven cases which remain for consideration are too few to merit detailed analysis. The result was good in three, fair in three, and bad in one. The latter required further surgery.

From a more extensive and more recent experience of this operation it is clear that complete relief of pain can be expected in perhaps two-thirds of patients, usually with retention of a reasonable range of hip movement. Much difficulty has been experienced with delay in union of the osteotomy. Occasionally it may never unite, though it may not give rise to symptoms. Indeed, the patient with the best result in the small group reviewed above showed no evidence of union of the osteotomy. This is a complication which is not mentioned in the reviews of Osborne and Fahrni (1950), Wardle (1955), and Adam and Spence (1958).

Acrylic Replacement of the Femoral Head

This operation was performed only during 1951 and 1952, and 46 hips were so treated. The 28 hip-joints which were re-examined appeared to give a reasonable indication of the results of the operations. Many of the other patients have replied to a letter, and some have stated that the joint is still satisfactory.

The review of these patients now covers a period of about six years, and the results are indicated briefly

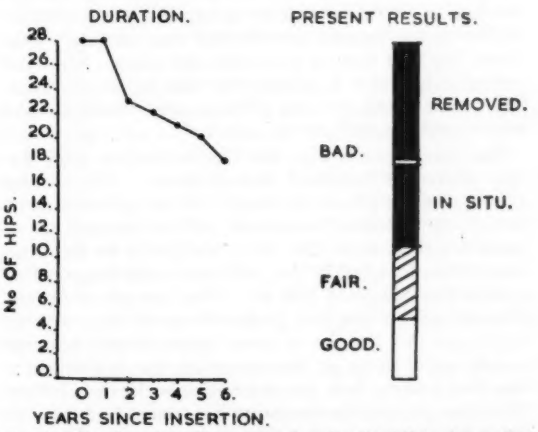

FIG. 3.—Results of acrylic prosthesis. On the left is shown the number of prostheses remaining in the hip at varying periods after the initial operation. Against those on the right are charted the results of the operation.

in Fig. 3. As time has passed there has been a steady diminution of the number of prostheses remaining in position and giving satisfactory service. Each year one or more of these patients require removal of the acrylic head.

At the present time five patients with unilateral operations retain a good result. These patients have a good range of hip movement, some of them walk without a stick, and none has any pain. There are six others who still appear to be better than pre-operatively, but all complain of pain and some have an unstable hip. The patients with a bad result are more disabled than they were pre-operatively: many of them require removal of the prosthesis, but are understandably reluctant to undergo further surgery. Regardless of the clinical condition of the hip, the radiographs all show gross erosion and ballooning of the acetabulum, often with necrosis of the neck of the femur and subluxation of the hip-joint.

It is unfortunate that there is no detailed information either of the state of the prostheses which were removed at operation or of the histological changes taking place around the hip-joint in those patients requiring further surgery. Indeed, the failure of the Judet prostheses has been considered by only one author (Pridie, 1955), and an analysis of the factors which have led to its disuse would clearly be of value. In view of the amount of fibrosis which forms around these hips it would appear that simple removal of the acrylic head with trimming of the neck might be sufficient to give some relief of pain with relative stability of the hip.

Cup Arthroplasty

Only 30 of the 72 cup arthroplasties performed during the years under review were available for re-examination. The type of mould used and the subsequent fate of the patients are indicated in Table IV.

TABLE IV.—*Cup Arthroplasty*

	Smith-Petersen	Crawford Adams	
		Acrylic	Metal
Good	6	2	
Fair	7	3	
Bad *In situ*	3	2	1
Bad Removed	4	1	2
Total	20	8	3

Though a small number of these patients have presented at a later date with symptoms severe enough for further surgery to be required, revision has been necessary only during the first year or two after operation. Thus the general impression is gained that this is the operation which will stand the test of time and in which late deterioration is unlikely to occur.

The good results with the Smith-Petersen cups are very impressive but quite unpredictable. There seems to be no way in which the results of these operations can be forecast. Roughly one-third will be expected to be good, one-third to be fair, and one-third to be bad; the results therefore fall in line with the much larger series analysed by Shepherd (1954b). The amount of flexion in these patients was 90+ degrees in seven, 60+ degrees in six, and 30+ degrees in three. Most of them retained a very useful range of hip movement, but in only three was this greater than the pre-operative level. Within this series at least, the operation has tended to retain the range of movement rather than to increase it. To some extent this must be due to the pre-operative selection of patients.

The two cups designed by Crawford Adams were used in 11 hips. The reaction of the hip to the presence of the acrylic concentric cup was very similar to its reaction to the Judet prostheses. The somewhat better results obtained with the cup are probably only due to its simplicity. The metal concentric cup was used on only three occasions; two of these had to be removed and the end-result in the third was bad. In the one specimen available for examination the cup had fractured.

Pseudarthrosis

In contrast to the other operative procedures, pseudarthrosis has been used in only a small group of patients who were considered unsuitable for the more ambitious reconstructions, and as a salvage procedure in the arthroplasty which had failed. These patients thus tend to form a selected group. In most of them the pseudarthrosis was supplemented by a subtrochanteric osteotomy. The numbers of patients involved are too small to show how the osteotomy influences the late results of a pseudarthrosis.

In the classification of the results of the pseudarthrosis a distinction has been drawn between operations performed as a primary or a secondary procedure. The results are shown in Table V.

TABLE V.—*Results of Pseudarthrosis*

	Primary	Secondary
Good	6	2
Fair	1	4
Bad	0	6

TABLE VI.—*Relief of Pain by Pseudarthrosis*

	Painful	Pain-free
Primary	6	1
Secondary	10	2

It is clear that there is a considerable difference between the results in these two groups. If the relief of pain alone is taken as a criterion of a successful operation the results are very similar (Table VI).

In some of these patients, however, the relief of pain was of secondary importance to the retention or the restitution of hip movements: the range of post-operative flexion was 90+ degrees in four, 60+ degrees in eight, 30+ degrees in five, and none in two.

The range of movements in these patients is not significantly different from those which have followed arthroplasty. After a pseudarthrosis, however, active hip flexion is usually lost, and some difficulty in lifting the leg may therefore be experienced. Some patients have found difficulty in driving a car. The shortening of the leg and the instability are usually minor difficulties which the patients rapidly accept, but most of them use a stick when walking out of doors.

Other Operations

Under this heading the following operations have been recorded: replacement arthroplasty (Stamm 3 and Moore 1), 4; Stamm acetabuloplasty, 1; and cheilotomy, 1.

Of the Stamm replacement arthroplasties, two became painful and the prosthesis was removed, and one remains in position with a relatively pain-free joint but some instability. The Moore arthroplasty is painful, with a small range of movement. The patient with the acetabuloplasty has a small range of hip movement but a little pain. The result of the cheilotomy is

disappointing, and the hip shows the changes of avascular necrosis. These cases are too few to merit more detailed consideration.

Secondary Operations

Revision has occasionally been necessary after all procedures except McMurray's osteotomy (recent experience has shown that this operation is not immune from complications). The results of these procedures are indicated in Table VII. The analysis has been limited to a simple determination of whether improvement or deterioration has followed the second operation.

TABLE VII.—*Results of Revision Procedure*

Primary Operation	Revision	No. of Cases	Improved	Unchanged	Worse
Arthrodesis	Rearthrodesis	1		1	
	McMurray's osteotomy	2	1	1	
Pseudarthrosis	Pseudarthrosis	1			1
	Trimming femoral stump	2	2		
Cup arthroplasty	Arthrodesis	1		1	
	Pseudarthrosis	4	1	3	
Acrylic prostheses	Pseudarthrosis	8	5	2	1
Metal prostheses	Arthrodesis	1		1	
	Pseudarthrosis	1	1		

From a limited experience of revision procedures, and also from a review of the disabilities occasioned by the failure to gain relief from a primary operation, the following general principles emerge.

Arthrodesis.—The pain and disability of a fibrous rather than a bony ankylosis are rarely severe enough to justify further operative procedures, particularly as these carry little chance of relieving symptoms. When the patient is young rearthrodesis may be attempted. This, however, is the age at which non-union is rare. In the elderly the problem of non-union is more common, but the prospect of achieving bony ankylosis by a second operation is correspondingly more slender.

Pseudarthrosis.—Relief of pain has been achieved in two patients by simple refashioning of the bone ends. This is a simple manœuvre—the period in hospital need only be short—and perhaps it deserves a wider application.

Arthroplasty.—Whatever type of arthroplasty has been performed, revision demands the removal of the prosthesis. These patients are often severely disabled, and Girdlestone's operation may relieve their pain. To supplement the operation by an osteotomy makes it a more lengthy procedure without adding materially to the final stability. Many of these patients have already developed what is effectively a pseudarthrosis from acetabular absorption, and are therefore adapted to the loss of hip stability.

It would appear that arthrodesis of the hip is rarely achieved after an arthroplasty has failed. In the younger patient, however, this might well be the procedure of choice.

Bilateral Arthritis of the Hips

Clinical and radiological evidence of involvement of both hips in an arthritic process does not necessarily indicate that both require surgical treatment. Indeed, if the more severely affected hip can be treated to provide a strong, painless leg, the other hip may be spared. It is generally thought that this can best be achieved by an arthrodesis.

When both hips have required treatment, either initially or during the follow-up period, a number of combinations of operations have been performed. The results of these procedures have already been recorded in discussing the fate of individual hips, and the final effect on the patient has therefore been assessed only in very general terms (Table VIII).

TABLE VIII.—*Bilateral Operations*

	Good	Fair	Bad
Arthrodesis and cup arthroplasty	1	0	2
,, ,, pseudarthrosis	1	0	0
Bilateral acrylic prosthesis	0	2	3
McMurray's osteotomy and pseudarthrosis	0	0	1
Acrylic prosthesis and pseudarthrosis	0	0	1
Cup arthroplasty and acrylic prosthesis	1	0	0
Bilateral cup arthroplasty	0	0	1
Total	3	2	8

It is probable that this is an unrepresentative series of patients. From the correspondence with those who failed to attend, the impression has been formed that very few patients with severe bilateral arthritis of the hips have gained relief. It is thus of the greatest importance to preserve the function of the second hip. That this may be done by arthrodesis of the more affected side has already been noted. Where surgical treatment of one hip has been unsuccessful the other hip will often deteriorate. Even a hip which was normal before its fellow was subjected to operation may show gross signs of degenerative arthritis within a few years.

Conclusions

In the treatment of the osteoarthritic hip arthrodesis remains the procedure of choice. Though bony fusion may be achieved in only two-thirds of the patients, pain from a fibrous ankylosis is rarely severe. In the young patient a stiff hip is a trivial disability; in the elderly it is more serious, and is occasionally a great handicap. Where relief of pain is complete it is acceptable; where a stiff hip is associated with a painful fibrous union the level of activity is often low. Over the age of 60 bony fusion has occurred in fewer than half the patients, and when to the risks of non-union are added the hazards of fracture of the femur the disadvantages of this operation in the elderly appear to be substantial. There is thus every justification for the search for a more acceptable procedure.

Cup-arthroplasty has given a measure of relief to patients with unilateral osteoarthritis of the hip, though the results, at least in terms of relief of pain, have been greatly inferior to those of arthrodesis. Nevertheless, there is a place for an operation which will retain mobility, particularly in the second hip, and in the elderly. It is unfortunate that these patients are frequently unable to manage the intensive and often lengthy period of rehabilitation which this operation demands.

The intertrochanteric osteotomy of McMurray probably offers a better chance of retaining a mobile, painless hip than any arthroplasty. Unfortunately the painful hip with a good range of movement is rarely seen. By the time the patient is sufficiently disabled to accept a period of three months or more in hospital the hip is usually stiff. Similar difficulties arise in its application to the problem of the second hip. Many of these patients manage for many years with an arthrodesis on one side; by the time the other hip requires operative treatment it is usually too stiff to respond to the osteotomy.

The value of the pseudarthrosis, apart from its place after a prosthesis which has failed, lies in the retention of a reasonable range of movement with some relief of pain. It must be accepted that neither of these is certain—indeed, perhaps no more certain than in a cup arthroplasty. Nevertheless, the retention of hip

movements depends less upon the active efforts of the patient, and it is therefore more suitable in the elderly. The results of the operation might be better if it were not so commonly applied to the grossly disabled patient.

None of these operations will enable a patient to escape from hospital much before three months have elapsed. In the elderly, time is of the greatest importance, and any procedure which entails a shorter stay in hospital demands consideration. This is the merit of the replacement arthroplasty. It must be accepted, however, that no prosthetic replacement of the femoral head in the arthritic hip has yet been shown to give a durable, stable, painless joint. To some extent this must be due to a failure of materials and design. Mere replacement of the femoral head, however, cannot be expected to relieve all pain and restore all movement. It may, however, provide an acceptable compromise between the disadvantages of the stiff hip and the perils of the formal arthroplasty.

These patients were under the care of Mr. J. S. Batchelor and Mr. T. T. Stamm. It is a pleasure to express my gratitude to them.

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GERIATRIC SURGICAL EMERGENCY

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In general, geriatric medicine may be regarded as embracing all patients over 50 years (Thewlis, 1946), but the major problems of surgical management in the geriatric patient are not seen with any frequency until a much greater age. By the age of 70, however, few patients fail to show unmistakable signs of physical or mental degeneration. It was therefore decided to review all the patients of 70 years and over admitted as emergency cases to a single surgical unit over a period of four years. It is not suggested that there is any essential pathological difference between the surgical diseases of patients under and over 70, but the treatment of these diseases in the aged often calls for some modification of standard practice, and geriatric surgery resolves itself into a series of compromises between the optimum surgical treatment required by the disease and the needs of a patient whose capacity to withstand treatment is rapidly diminishing. To emphasize this aspect of the management of the geriatric surgical emergency, a system of classification has been used which compares the programme of treatment provided for the patient with that which would have been offered to a fit man of 50 years with comparable pathological condition.

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Classification

Group 1: Optimum Management.—a, No operative treatment required. *b,* Full optimum operative treatment provided.

Group 2: Compromise Management.—a, Emergency surgery not required. Unfit for desirable elective surgery. *b,* Emergency or palliative surgery provided. Unfit for desirable elective surgery. *c,* Emergency or palliative surgery provided. Lesion otherwise inoperable by ordinary surgical standards.

Group 3: Unsatisfactory Management.—Unfit for emergency or palliative surgery.

Present Series

During the four-year period from August, 1954, to August, 1958, 408 patients of 70 years or over were admitted as emergency cases to a unit of 70 beds, or were transferred to it as emergencies from medical beds. The details are summarized in Table I. It will be seen

TABLE I.—*Summary of Whole Series of* 408 *Cases*

Group	No. of Cases	Male	Female	Deaths		Average Age in Years	Average Days in Hospital	No of Cases with Medical Complications
				No.	%			
Misdiagnoses	35	24	11	7	20	77	12	—
Strangulated hernia	73	38	35	9	12	79	12	28
Malignant obstruction	23	13	10	11	48	73	28	8
Simple ,,	20	10	10	6	30	78	21	7
Appendicitis	29	12	17	6	21	77	23	11
Diverticulitis	16	10	6	1	6	72	19	4
Biliary disease	37	17	20	5	14	77	13	15
Perforated peptic ulcer	8	6	2	2	25	86	27	5
Other gastric lesions	16	7	9	4	25	77	26	5
Pancreatitis	6	3	3	2	33	73	10	1
Retention of urine	118	118	0	34	29	77	32	70
Vascular lesions	10	6	4	8	80	77	13	5
Miscellaneous	17	10	7	9	53	75	14	7
Total (excl. 35 misdiagnoses)	373	250	123	97	25	77	22	166 (45%)

Total number of operations = 185. Operative deaths = 54 (29%).

that a group of 35 cases is described as misdiagnoses and is excluded from the total analysis. These cases were admitted with a surgical diagnosis but subsequently proved to have no surgical disease and were either discharged or transferred to medical units. Of these 35 patients, 8 were admitted for intestinal obstruction but were proved to have constipation or faecal impaction, 3 were sent in for retention of urine because of the oliguria of congestive cardiac failure, 12 diagnosed as cases of perforated peptic ulcers had either coronary occlusions or exacerbations of peptic ulcers, while the remainder included such diverse conditions as retention of urine in a woman with diabetic polyneuritis, a myeloid leukaemia with abdominal pain, a case of Paget's disease of bone, and a patient with an aneurysm of the thoracic aorta. The mortality of this group during an average stay of 12 days was 20%, making an interesting comparison with the surgical conditions summarized in the rest of Table I.

A few other general comments are necessary. The ratio of 250 male cases to 123 female almost exactly reflects the proportion of 2 male beds to 1 female bed which exists in this unit. The male predominance was due almost entirely to cases of urinary retention, so that in other sections of the table the sex incidence is probably a reasonably accurate reflection of the natural ratio for the disease concerned. The deaths were those occurring in hospital from any cause, and, while it was

not thought worth while to complicate the table with separate operative and non-operative mortalities in each condition, the total number of operations and the operative mortality are included in the final summary.

Turville and Dripps (1948) record 1,064 anaesthetics given to patients of over 70 with 4.9% mortality. Against this a mortality of 29% among patients operated upon may sound a discouraging figure, but the present series, exclusively composed of emergency cases, includes a high proportion of major procedures, and takes account of all deaths in hospital whatever the cause. Moreover, it implies that 70% of patients aged 70 to 90 years subjected to major operations, often in the presence of important medical complications and under emergency conditions, survived to leave hospital. The average stay in hospital was 22 days. This figure includes those who died, as well as those discharged, so that the time in hospital must be considered in conjunction with the mortality for the corresponding condition, as a high mortality tends to shorten the average length of stay.

The medical complications referred to in Table I are those present on admission and not any developing in hospital. Minor disorders were disregarded and medical complications were included only if their severity would significantly influence the approach to the case. The chief conditions found were hypertension (with pressures above 180/100), chronic bronchitis and emphysema (with notable dyspnoea and productive cough), congestive cardiac failure, fibrillation, aortic or mitral valvular disease, previous coronary occlusion or effort pain, previous cerebrovascular accident, paralysis agitans, and major arthritis, especially if treated with steroids. In all, such complications were present in 45% of the cases, confirming the view of Cates (1959) in haematemesis, that in elderly patients associated conditions are as great a hazard as the primary disease.

In the general surgical management of these patients the investigation and treatment have been restricted to the essential minimum. Major dehydration or electrolyte disturbance may make intravenous correction unavoidable, but "it is better for intravenous injections to err on the side of giving less than giving more" (Elman, 1952). While the risks of dehydration are obvious in the elderly, the effect which drips produce—of tethering in immobility a patient already reluctant to move and of depressing his spirits with discomfort and anxiety—is insufficiently regarded. Rectal or subcutaneous routes for fluid administration are often effective, and at times a compromise with ideal fluid-balance requirements in the interest of an active patient may be well worth while. The amount of good which can be done for most of the medical complications during the brief period available before an emergency operation is small, but rapid digitalization of a fibrillating patient in early congestive failure may make an impossible risk eminently possible. Where more time can be gained, chronic bronchitis and congestive failure may be greatly improved. The place of antibiotics in the treatment of chest complications before and after operation is obvious, but of equal importance is a nursing staff trained to insist on frequent breathing exercises and coughing. Finally, in maintaining the will to live, which is so important in the elderly, there is no substitute for the mixture of sympathy and cajolery provided by an experienced ward sister.

The need for skilled anaesthesia by staff experienced in managing elderly patients cannot be overemphasized. Such a service has been constantly available to the cases in this series, and those rejected for operation have been rejected by the surgeon rather than by the anaesthetist. Criteria for assessing suitability for anaesthesia broaden rapidly when working among this type of patient. Where advantage can be taken of local anaesthesia, it is often wise to do so, strangulated hernias, in particular, lending themselves to surgery under a local block. The mortality does not seem to be much affected, but the convalescence after local anaesthesia appears to be smoother and quicker, possibly because local anaesthetics encourage speed and gentleness in the surgeon, qualities of particular importance to elderly patients. These patients do not stand prolonged operations well, especially under emergency conditions, and there is no substitute in their management for expedition on the operating-table.

Strangulated Hernias

The 73 cases (38 male, 35 female) had an overall mortality of 12%. There were 29 inguinal, 38 femoral, 4 umbilical, 1 incisional, and 1 obturator among them. In eight no operation was performed; of these, one with sloughing colon in an umbilical hernia was moribund on admission, one difficult incisional hernia was effectively reduced, and six inguinal hernias in unfit patients were successfully treated by taxis and a truss. For patients with inguinal hernias undergoing operation it was a frequent practice to obtain consent for orchidectomy in advance, as the speed and security of surgical treatment was increased by removal of the testis, especially in fat patients or in those with hernias with large sacs.

The advantages of a virtually subcutaneous operation easily performed under local anaesthesia with minimum trauma to muscle appear to outweigh the more direct access to the neck of the sac provided by the Lotheissen operation, especially in elderly patients. When resection was essential, and general anaesthesia was strongly contraindicated, it was quicker to supplement the low approach by a small paramedian incision rather than to disrupt the inguinal canal, even this being possible, with great gentleness, under local anaesthesia. Patients needing operation for their hernias under local anaesthesia were seen in advance by the anaesthetist and premedicated and prepared for operation as if for a general anaesthetic, so that in cases needing resection a change of method could safely be introduced during the operation. Among the 65 cases operated upon there were eight bowel resections with two deaths (25%), while 26 cases were done wholly under local anaesthesia and 37 had all or a major part of their operation under general anaesthesia. All the femoral hernias were explored initially by the low route, and the approach was modified only if bowel required resection.

Malignant Intestinal Obstructions

All 23 patients in this group were suffering from carcinoma of the colon or rectum, and only one, who was moribund on admission, was refused any surgery. In 15 patients only palliative surgery by colostomy or ileotransverse anastomosis was performed, but the remaining seven had initial decompression, subsequent resection, and anastomosis, and, where appropriate, closure of colostomy. Of the 22 patients operated upon, 10 died (45%), of whom seven were among the palliative

operations (48%) and three among the radical procedures (43%), a noticeably similar result with each form of treatment. The summary of the form of treatment compared with the optimum appears in Table II,

TABLE II.—*Comparison of Treatment Given with Theoretical Optimum*

Group:	1a	1b	2a	2b	2c	3
Strangulated hernia	—	65	7	—	—	1
Malignant obstruction	—	7	—	9	6	1
Simple "	—	14	3	2	—	1
Appendicitis	—	24	4	—	—	1
Diverticulitis	7	—	1	7	—	1
Biliary disease	—	6	25	4	—	2
Perforated peptic ulcer	3	4	—	—	—	1
Other gastric lesions	—	10	—	4	—	2
Pancreatitis	2	4	—	—	—	—
Retention of urine	13	75	—	14	—	16
Vascular lesions	—	5	—	2	—	3
Miscellaneous	1	7	2	1	1	5
Total	26	221	42	43	7	34
Percentage of whole series (373)	7	59	11	11·5	1·9	9

and it should be noticed that in six patients given only palliative treatment the tumour would have been regarded as inoperable in a 50-year-old man, but that in nine cases only palliative surgery was offered to patients with resectable growths because of age or infirmity.

Simple Intestinal Obstruction

The results in this group are particularly disappointing. Of 20 patients (10 male, 10 female), one was moribund on admission, but 16 of the remainder were operated upon, with five deaths, a mortality of 31%. The cases undergoing operation included eight adhesion obstructions, two of which required gut resections, three internal hernias, one intussusception of ileum due to a lipoma, and one gall-stone ileus. The remaining six cases had volvulus of the sigmoid colon, a condition treated conservatively by tube decompression when diagnosed (Bolt, 1956). In three of these, however, laparotomy was performed, one having a Mikulicz operation and the others a simple untwisting of the volvulus with a temporary sigmoid colostomy.

Though the overall mortality of 30% was well below that for malignant obstruction, deaths in the simple cases are clearly of even more moment than in the malignant cases. These patients suffer from the general reluctance to diagnose emergency abdominal conditions in the elderly, consequently they come in too late, with a degree of distension and dehydration which makes subsequent management very difficult. When patients present early and can be operated upon promptly without long periods of drip and suction, even very elderly patients do remarkably well. The mortality quoted by Cooke (1958) for simple intestinal obstruction at any age was 21%, with which a mortality of 30% in patients over 70 years of age does not compare too unfavourably, but both figures suggest the paramount need in these cases for early surgical treatment.

Appendicitis

Of the 29 patients in this group (12 male, 17 female), six died (21%). One of these was considered unfit for any surgery, one died while undergoing conservative treatment for an appendix abscess, and the remaining four died after operation, an operative mortality of 17%. Three patients who recovered from appendix abscesses under conservative management were not advised to have elective surgery later, as the risk of operation was thought to exceed the risk of recurrent appendicitis during their life expectancy, and so far none has returned with a recurrence. Of the 29 cases, 20 (69%) were perforated upon admission: the perforation rate among unselected appendicitis admitted to the unit is 17%. The high rate of perforation agrees with the experience of Christensen (1958) and reflects both the trivial signs and symptoms produced in the elderly by major abdominal pathology and the general reluctance to diagnose appendicitis in old people. The teaching that acute appendicitis is rare in the aged is inaccurate and should be abandoned.

Diverticulitis

There were only 16 cases of diverticulitis in the series, a number too small to be significant. This may explain the low mortality of 6%, which does not correspond with the general experience that diverticulitis provides some of the most difficult problems of management encountered in emergency surgery. Of the 16 cases, seven had local inflammatory masses in the left iliac fossa or pelvis resolving on conservative management, five had peritonitis or an abscess, two had vesico-colic fistulae, and two had intestinal obstruction. The analysis of the type of treatment offered, compared with the optimum, is to be seen in Table II, where the emphasis on palliation at this age is evident. Seven patients treated conservatively and offered no definitive surgery had lesions which might reasonably have been treated on similar lines in young patients, but one patient in group 2a who had no emergency treatment should optimally have had a cold resection subsequently, while the seven in group 2b would not have been left with permanent colostomies at 50. Probably no two surgeons would make quite the same choice of patients for resection in diverticulitis, and the classification consequently reflects the practice of the unit, but very few patients over 70 have a physique which justifies elective resection of the colon for a non-malignant condition, especially as the stronger the indication for resection the greater the technical difficulty.

Biliary Disease

Most acute biliary conditions may be regarded as urgencies rather than emergencies, but they are commonly admitted as emergencies, as were the 37 cases considered here, of which 29 had acute cholecystitis or biliary colic, and eight had obstructive jaundice. It has not been the practice of the unit to indulge in emergency cholecystectomy, certainly not at this advanced age, and emergency operation was performed in only four cases, three because of deterioration on conservative management, and one because of a diagnostic error. In each case cholecystotomy, with removal of stones, was performed, and one patient died (25%). The majority of patients treated conservatively for acute cholecystitis had subsequent cholecystography, but it has not been the practice to offer elective cholecystectomy for proved stones in this age group. Successful cholecystectomy has occasionally been performed for a patient with severe recurrent symptoms, but the frequency of serious recurrence has not been sufficient to suggest that the need for surgery usually outweighs the high operative risk. Lee (1958) suggests that gall-stones *per se* are not a danger to life nor an indication for cholecystectomy, and in the higher age groups this appears to be true, as the chance of further major complications is not great within these patients' expectation of life.

Of the eight patients with obstructive jaundice an exploratory operation was performed on five—four while jaundiced and one subsequently—and all had stones removed from the common bile duct, with or without cholecystectomy; two died, giving an operative mortality of 40%. The remaining three included one patient with carcinoma of the pancreas dying of liver failure without surgery, and two patients with unmistakable obstructive jaundice, resolving spontaneously, who were not regarded as fit subjects for elective surgery. The mortality over the whole biliary group was 13.5%, but the operative mortality was 30%, reflecting the fact that the least favourable cases eventually demand surgery.

Perforated Peptic Ulcer

There seems at the moment to be a noticeable decline in the incidence of perforation of peptic ulcers, and the condition is becoming a relative rarity among abdominal emergencies. Consequently there were only eight cases in this group—three gastric ulcers, four duodenal ulcers, and one an anastomotic ulcer following gastro-enterostomy. The average age of this group was the unusually high one of 86 years, and two patients died, a mortality of 25%. Of the eight cases, one was moribund and beyond help, while four were operated upon and had simple closures of their perforations with one death. The remaining three were treated conservatively despite clear evidence of perforation, including free gas beneath the diaphragm in *x*-ray films, and all these did well. There seems to be a particularly useful place for conservative management of elderly patients with perforated peptic ulcers who are bad operative risks. In cases otherwise suitable for non-operative treatment liberal free gas has not appeared a contra-indication: a woman of 92 years, with each half of her diaphragm harbouring large amounts of gas, did particularly well on a medical regime.

Other Gastro-duodenal Emergencies

There were 16 cases in this group, nine with haemorrhage, and seven with pyloric obstruction. Of the nine with haemorrhage, seven had emergency partial gastrectomy, one who was bleeding from an anastomotic ulcer after gastro-enterostomy and whose duodenum appeared normal had his ulcer excised and the stoma closed, while the other died without becoming fit for surgery. Of the seven patients with pyloric stenosis, four were due to carcinoma and three to simple ulcers; three of the carcinoma patients had partial gastrectomy, and the three with simple stenoses had gastro-enterostomy, the remaining patient dying without surgery. The total mortality for the whole group was four (25%), but there were only two deaths after 14 operations, a mortality of 14%.

Pancreatitis

There were only six cases of acute pancreatitis, with a mortality of 33%. In two cases in which a firm diagnosis was made without operation the serum amylase was convincingly high, but as both patients recovered satisfactorily the diagnosis was not absolute. The remaining four were diagnosed at laparotomy and no further manœuvre was performed; but, despite this, two died—an operative mortality of 50%.

Retention of Urine

This constitutes the largest single group of cases, 118 in all, and presents a wide variety of problems in management. Many were admitted in a hopeless condition, the retention arising as a terminal event in a serious medical illness and presenting problems of management insuperable at home. They were then admitted to a surgical ward as cases of retention of urine, and help to explain the 60% incidence of medical complications in this group on admission, and a mortality of 29% for the group as a whole compared with 15% among those subjected to major surgery.

Of the 118 cases, 88 had benign prostatic enlargement, 25 had carcinoma of the prostate, four had strictures, and one had carcinoma of the bladder. Sixteen were treated by catheterization only and either succumbed rapidly to associated medical disease or, on becoming ambulant again, after recovery from medical conditions were able to pass urine effectively. None of these was suitable for elective prostatectomy, and when able to pass urine satisfactorily they were discharged. In 13 of the cases with carcinoma of the prostate, catheterization followed by stilboestrol and eventual removal of the catheter proved adequate, and they were discharged with adequate micturition for subsequent follow-up; in two of them stilboestrol was supplemented by castration. In nine cases transurethral resection followed by stilboestrol re-established micturition, but in three others who failed to respond to hormone therapy, even transurethral surgery was considered too hazardous and permanent suprapubic drainage was performed.

Apart from those treated solely by catheter drainage, 11 benign obstructions were regarded as fit only for permanent suprapubic cystotomy. This decision was taken with reluctance, and only after a considerable period of catheter drainage and energetic treatment of associated medical disease. Consequently it is unlikely that any of them will subsequently be considered fit for major surgery, and, in fact, no second-stage operation has been done in the whole series. Major prostatic surgery has been performed on 64 of the benign cases, 52 having retropubic prostatectomies, two having transvesical operations because of associated bladder disease, and 10 transurethral resections, using the McCarthy resectoscope. In the early cases of the series, low spinal anaesthesia was supplemented with light general anaesthesia, but, more recently, epidural anaesthesia similarly supplemented has been used consistently and found highly satisfactory. The details have been discussed elsewhere by Morris and Candy (1957). The operative mortality in these cases, together with the nine carcinoma patients having transurethral resections, was 11 in 73 cases, or 15%.

It has not been the practice to do emergency prostatectomies. The opposing views on this subject are well known, but we have been influenced both by the high rate of associated disease in these patients, demanding pre-operative treatment, and by the belief that a few days in the ward under supervision, growing accustomed to staff, surroundings, and routine, benefit these elderly and often feeble patients more than does the avoidance of pre-operative catheterization. More leisurely pre-operative assessment and corrective measures greatly benefit them, and it is not apparent that catheter drainage makes an important contribution to mortality or morbidity in this series, or that major

surgery, precipitously arranged at inconvenient hours, would add much to the patients' prospect of recovery.

Vascular Lesions

These cases are included in the interest of completeness. Of the 10 patients, four had major limb gangrene on admission, and all died, with or without amputation, one had mesenteric occlusion, and three had leaking aortic aneurysms, and all died. The only survivors were two patients who underwent local amputation of gangrenous toes.

Miscellaneous

This group allows no useful analysis, as it contains such varied conditions as bleeding colonic neoplasms, polyposis of the ileum, and a wide variety of abscesses, the total of 17 cases including nine operations with four deaths and an overall mortality of 53%.

Adequacy of Treatment

The comparison of treatment provided with the theoretical optimum is summarized in Table II. It will be seen that 26 patients (7%) needed no operative treatment, and that a further 221 (59%) received operative treatment which could be regarded as optimum for their condition, so that a total of 247 cases (66%) received fully adequate treatment. It would perhaps be legitimate to add to these the seven cases of group 2c who were inoperable on pathological grounds, so as to complete the group in whom age and associated disease did not prevent an adequate programme of treatment—68% of the total. In 85 patients (23%) palliation only was possible, and elective surgery was considered to be unjustifiable on grounds of age or general health, while a further 34 (9%) had to be rejected even for emergency measures. Thus in 119 cases (32%) the programme of treatment was notably inadequate to deal with the known pathology.

Clearly, the decision on whether to accept or reject a particular patient for radical surgery is a very difficult one, and is often best taken after assessment of the patient by physician and anaesthetist, as well as surgeon, and a joint discussion of the findings. The surgeon will be influenced by his personal experience of the disease in question, the facilities at his disposal, the views expressed by his colleagues on the general health of the patient, and by his own assessment of the patient's morale. Consequently, different surgeons would select differently, and a ratio of one patient in three rejected for radical surgery may be thought to err towards the conservative, but it is also an illustration of the increasing place of the elderly and unfit among the general surgeon's patients and of the difficult decisions involved in giving them an adequate surgical service.

Summary

A study is presented of 408 emergency surgical cases in persons over 70 years of age admitted to one surgical unit during a four-year period.

The cases are reviewed in disease groups, and the management and outcome are discussed.

A system of classification comparing treatment provided with a theoretical optimum is described and applied.

My thanks are due to Mr. W. J. Ferguson, under whose care all these patients were admitted, for permission to make and publish this study, and to Dr. M. W. Warren, consultant geriatrician at the West Middlesex Hospital, for much helpful advice. I am also indebted to the records officer and his staff at the West Middlesex Hospital for their great help in tracing records.

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HYPOGLYCAEMIA IN METASTATIC FIBROSARCOMA OF THE LIVER

BY

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The association of primary carcinoma of the liver with hypoglycaemia was originally observed by Nadler and Wolfer (1929). The subject has since been carefully reviewed by McFadzean and Yeung Tse Tse (1956), who reported nine cases of this disorder in a personal series of 25 patients with malignant hepatoma. Reports on the association of hypoglycaemia with secondary tumours of the liver are rare. Wilder (1927) mentioned two cases, without giving details. Bielschowsky (1932) observed hypoglycaemia in a patient with hepatic metastases from carcinoma of the stomach, and Irsigler (1934) found increased insulin sensitivity, but no frank hypoglycaemia, in patients with liver metastases from cancer of the rectum. Himsworth (1943), in a review of hypoglycaemia, mentioned secondary carcinoma of the liver as one of the causes without giving other details. Hines (1943) reported on a patient with a retroperitoneal liposarcoma who had hypoglycaemic attacks which ceased when the sarcoma was removed and recurred a few years later when hepatic metastases developed. Among Mellinkof and Tumulty's (1952) series of 20 patients with hepatogenic hypoglycaemia were two with metastatic liver cancer and biliary cirrhosis due to obstruction by the primary pancreatic tumours. The metastases were small and the diffuse cirrhotic process was obviously responsible for hypoglycaemia. Holten (1957) described the case of a patient with a metastatic spindle-cell sarcoma of the liver who had hypoglycaemic attacks five years after removal of the primary growth.

The following case was one in which extensive metastatic involvement of the liver from a gastric fibrosarcoma gave rise to recurrent hypoglycaemic attacks.

Case Report

This 70-year-old man was admitted to hospital in coma on November 23, 1957. He was a known diabetic and had been treated with daily insulin for six years. For four months he had been showing increasing anorexia, weakness, tiredness, and loss of weight, and his insulin requirements decreased, 20 units of protamin insulin being given on alternate days instead of every day. His last injection had

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been 36 hours before admission. In the evening preceding admission he showed some confusion and disorientation, and in the early morning of the same day he was found in coma.

On examination he was comatose and pale, but well nourished. Spontaneous hyperkinesia was present. His eyes were wide open and did not respond to visual stimuli, but the pupils reacted normally to light. Superficial and tendon reflexes were normal. His temperature was 95° F. (35° C.), pulse rate 104, and B.P. 120/80. His heart was fibrillating, but the jugular venous pressure was normal. Scattered fine rales were heard at both bases posteriorly. His liver was slightly enlarged, with a firm border. Under the border of the liver and at the mid-clavicular line a hard oval mass was palpable moving downwards with inspiration. The spleen could not be felt. Dullness in the flanks was due to fluid, an aspirated specimen of which proved to be transudate (no tumour cells were subsequently demonstrated on cytological examination). His bladder was not distended and a catheter specimen of urine was free of sugar and acetone. There was also gross oedema of both legs.

On balance it was felt that the patient was in hypoglycaemic coma, it being assumed that because of neoplastic disease even small amounts of insulin might be causing hypoglycaemia. The blood-sugar was found to be 39 mg./100 ml., and 100 ml. of 35% glucose was infused intravenously. At the end of the infusion the patient regained consciousness and could answer questions. Other laboratory findings were: haemoglobin, 11.8 g./100 ml.; W.B.C., 8,000; blood urea, 32 mg./100 ml.; bilirubin, 0.4 mg./100 ml.; total cholesterol, 94 mg./100 ml.; alkaline phosphatase, 32 K–A units; $ZnSO_4$, thymol, and cephalin-cholesterol tests were normal. Chest radiographs showed a small triangular collapsed area at the right middle lobe and a plain radiograph of the abdomen revealed gross displacement of the ascending colon to the left. Because of his extreme weakness further investigations were postponed. But in view of the laboratory findings (alkaline phosphatase) it was thought that the liver might be involved in the neoplastic process and that the palpable mass was arising from the liver.

A diet rich in carbohydrates was prescribed, with only partial success because of obstinate anorexia. Later the fasting blood-sugar level was 60 mg./100 ml. on November 24, 53 mg. on the 26th, and 69 mg. on the 28th, and there were no signs of hypoglycaemia. The patient seemed to be improving. On December 1 blood was withdrawn at 9 a.m. for routine examination, and he seemed very well. An hour later he was found in coma: 5% glucose, with hyaluronidase and adrenaline, was given by injection, but he died soon afterwards before phlebotomy could be performed. The blood glucose was subsequently reported to be 33 mg./100 ml.

At necropsy (limited to the abdomen) the liver weighed 2,100 g. and was seeded with numerous metastatic white nodules of variable size (Fig. 1), some of which were umbilicated. The largest nodule measured 11 by 9 by 8 cm. and projected fist-like from the lower surface. Neoplastic tissue had largely replaced the liver parenchyma. A growth measuring 9 by 7 by 5 cm. was found in the cardiac region of the stomach and the adjacent part of the great curvature. The growth projected mainly outwards, covered by serosa, and less towards the lumen, where the mucosa was ulcerated over a small area. The cardio-oesophageal lymph nodes and those along the lesser curvature were infiltrated by neoplastic tissue.

The main growth as well as the hepatic and lymph-node metastases presented essentially the same histological picture (Fig. 2)—numerous spindle cells with relatively infrequent mitoses and a varying amount of fibrous tissue between the cells, ranging from a few collagen fibrils to dense collagenous fibrous bands. The whole picture was very suggestive of fibrosarcoma.

The pancreas showed some increase in connective tissue, with lymphocyte infiltration and some atrophy of Langerhans' islets. The suprarenals were normal.

Discussion

It seems probable that the metastatic involvement of the liver was mainly responsible for the hypoglycaemic attacks in this case. Some doubt remains, however, whether this was the only factor, because the macroscopic appearance of the liver suggested gross but perhaps not critical reduction of liver parenchyma. The possibility of the tumour itself producing hypoglycaemia must therefore be considered. Fibrosarcomata and other sarcomata have been reputed to cause hypoglycaemia (Scholz *et al.*, 1957). Previously it had been thought on histological grounds that these tumours were in fact atypical islet-cell tumours (Skillern *et al.*, 1954), a hypothesis which was readily accepted by Holten (1957) as the explanation of the hypoglycaemia in his case of metastatic liver fibrosarcoma. Scholz *et al.* (1957) contested this view, and eventually August and Hiatt (1958) found insulin activity in their patient's tumour, which they regarded as a proved fibrosarcoma.

FIG. 1.—The anterior surface of the liver. The large nodule is seen to be projecting from the lower surface.

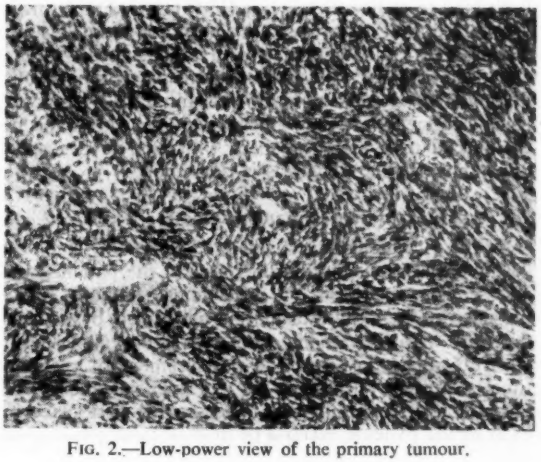

FIG. 2.—Low-power view of the primary tumour.

Another possible cause of the hypoglycaemia might be the diversion of blood glucose from the pathway of peripheral utilization to the tumour cells with their increased metabolic demands. This mechanism was well described by McFadzean and Yeung Tse Tse (1956) in their report on primary hepatomas.

Failure to recognize the exact cause of the low blood-sugar before death, the severity of the patient's illness, and the short period of survival in hospital prevented the completion of investigations which might have helped in elucidating some of the metabolic abnormalities in this case.

I am deeply indebted to Professor B. Malamos for permission to report this case and for his helpful criticism, and to Professor D. Eleftheriou for the histological report.

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RADIOACTIVE IODINE STUDIES IN THE DIAGNOSIS OF HASHIMOTO'S THYROIDITIS

BY

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Hashimoto's thyroiditis has recently been the subject of extensive investigation. Most workers have studied the immunological and biochemical abnormalities associated with this disorder, but relatively little attention has been paid to radioactive iodine (^{131}I) tests. Though it is recognized that these may produce abnormal results, attempts to evaluate their use in the diagnosis of the condition have been infrequent. This paper reports our findings in 41 patients with Hashimoto's thyroiditis using routine ^{131}I tests. Our experience with some of the special tests that have been suggested to be useful in establishing the diagnosis is recorded.

Subjects and Methods

Of the 41 patients investigated, 18 were euthyroid and 23 hypothyroid. The thyroid status of the patients was assessed on the basis of the clinical findings. The presence of hypothyroidism was confirmed by estimations of basal metabolic rate and serum cholesterol, electrocardiography, and the measurement of reaction time (Murray, 1958). A tentative diagnosis of Hashimoto's thyroiditis was made in the first place in each of the patients because of firm or hard generalized thyroid enlargement. It was confirmed either by histological examination or by the finding of biochemical abnormalities (Luxton and Cooke, 1956) and positive precipitin tests (Goudie *et al.*, 1957).

Routine ^{131}I studies were carried out in all patients. The gland uptake of ^{131}I was measured by a shielded scintillation counter at 24 or 48 hours after the oral administration of 25 μc of ^{131}I. The serum protein-bound ^{131}I (P.B.^{131}I) was measured by the resin-extraction method of Zieve *et al.* (1956) on a blood sample withdrawn at 48 hours. The butanol-extractable fraction was estimated after four washes of a serum sample by twice its volume of butanol after the *p*H had been adjusted to 2. Scanning of the neck was carried out by placing a shielded end-window Geiger counter in direct contact with the neck, expressing the results as counts/$\frac{1}{2}$ min./10 μc.

In seven patients with Hashimoto's thyroiditis and in 14 control patients with thyrotoxicosis or non-toxic goitres, studies were carried out after an intravenous tracer dose of ^{131}I (Berson *et al.*, 1952). 25 μc. of ^{131}I was injected intravenously and the rate of uptake by the thyroid gland was measured at regular intervals for 30 minutes. After the administration of 600 mg. of potassium perchlorate orally, the uptake was measured for a further 30 minutes. The uptake at the end of this period was expressed as a percentage of the uptake just before the administration of perchlorate. In six euthyroid subjects with Hashimoto's thyroiditis, the routine ^{131}I studies were repeated after the administration of L-thyroxine sodium in daily doses of 0.2–0.3 mg. for periods varying from 10 days to 20 weeks.

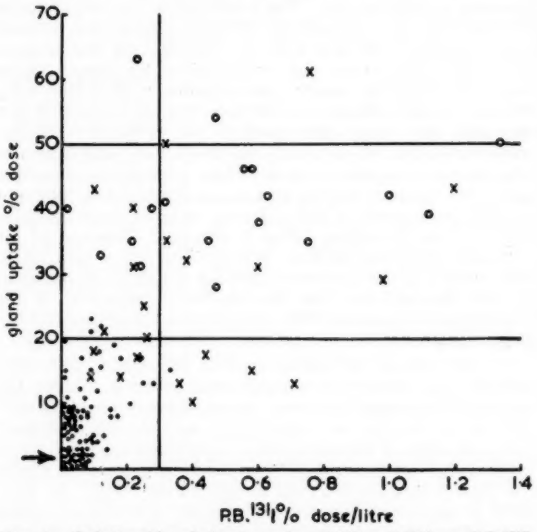

FIG. 1.—Relationship of gland uptake of ^{131}I and 48-hour P.B.^{131}I in patients with primary myxoedema and Hashimoto's thyroiditis. The arrow shows the position of the fifth patient with uptake below 20%. ●=Primary myxoedema. ×=Myxoedematous Hashimoto. ○=Euthyroid Hashimoto.

Results

The results of the routine estimations of gland uptake and serum P.B.^{131}I are shown in Fig. 1, together with the findings in 85 proved cases of primary myxoedema. It was found that there was no significant difference in the results between the uptakes at 24 hours and 48 hours, and they have been included together. Only

three of the 85 cases of primary myxoedema had gland uptakes greater than 19% of the dose, compared with 13 of the 23 hypothyroid patients with Hashimoto's thyroiditis. Of the 18 euthyroid cases of Hashimoto's thyroiditis, 16 had uptakes in the normal range of 20% to 50% of the dose; two of them had an uptake greater than 50%.

In 24 of the Hashimoto patients the 48-hour serum P.B.^{131}I was greater than 0.3% of the dose per litre. This comprised 12 each of the hypothyroid and euthyroid groups. Only one of the patients with primary myxoedema had a P.B.^{131}I above 0.3% of the dose per litre. This subject had a positive precipitin test and a palpable thyroid isthmus, and might therefore be considered to be a case of Hashimoto's thyroiditis.

TABLE
Distribution of Gland Uptake and 48-hour P.B.^{131}I

	Gland Uptake of ^{131}I (% of Dose)			Serum P.B.^{131}I (% of Dose/Litre)	
	<20	20–50	>50	<0·3	>0·3
Primary myxoedema (85 cases)	82	—	—	81	1
Hashimoto's thyroiditis:	—	3	—	3	—
Hypothyroid (23 cases)	10	—	—	5	5
	—	12	—	6	6
	—	—	1	—	1
Euthyroid (18 cases)	—	16	—	5	11
	—	—	2	1	1

When the results of the gland uptake and serum P.B.^{131}I tests are compared in the patients with Hashimoto's thyroiditis (see Table) it can be seen that all of the 18 euthyroid patients had a thyroid uptake of more than 20%—in six the P.B.^{131}I was normal and in 12 it was above 0.3% of the dose per litre. The P.B.^{131}I was normal in five and elevated in five of the 10 hypothyroid patients in whom the thyroid uptake of ^{131}I was less than 20%. It was normal in six and elevated in seven of the 13 hypothyroid patients in whom the thyroid uptake of ^{131}I was above 20%.

In the three patients studied the butanol-extractable fraction of the total serum ^{131}I was 57.6% (0.26% of the dose per litre), 51.0% (0.87%), and 45.0% (0.14%). These values showed that a significant proportion of the total P.B.^{131}I was butanol-insoluble, as the respective results for P.B.^{131}I were 0.47%, 1.56%, and 0.31% of the dose per litre.

The administration of potassium perchlorate to the 14 patients with non-toxic goitres or untreated thyrotoxicosis resulted in a block of further uptake in 10. A typical example is shown in Fig. 2a. In three the perchlorate had no effect, and in one there was a slight decrease in the uptake signifying discharge of radioiodine. In this patient the uptake 30 minutes after the drug was 94% of the value just before its administration. In all the seven patients with Hashimoto's thyroiditis the discharge of ^{131}I from the thyroid gland was pronounced (Fig. 2b), ranging from 12% to 21%.

The onset of the effect of perchlorate varied from within two to three minutes (recorded as "early") to 16 minutes, being more rapid in the Hashimoto group. The variation in this period may be related to absorption, as no precautions as regards fasting were taken.

It can be seen from Fig. 3 that the administration of thyroxine resulted in marked suppression both of the gland uptake of ^{131}I and serum P.B.^{131}I in all of the six patients studied. This effect was achieved with doses of thyroxine varying from 0.2 mg. to 0.3 mg. daily given during periods of 10 days to 20 weeks.

Discussion

In previous reports of radioactive iodine studies in Hashimoto's thyroiditis more attention has been paid to the results of the gland uptake of ^{131}I than to the serum P.B.^{131}I. There seems to be general agreement that the gland uptake may vary greatly (Skillern *et al.*, 1956; Doniach and Hudson, 1957; Furr and Crile, 1954; and Beare, 1958). In the present series the uptakes ranged from 2% to 64%, lying within our normal range of 20% to 50% in 16 of the 18 euthyroid patients and in 12 of the 23 hypothyroid patients. In three patients (two euthyroid and one hypothyroid) the uptake exceeded the upper limit of normal. Both Skillern *et al.* (1956) and Doniach and Hudson (1957) noted that there was poor correlation between the

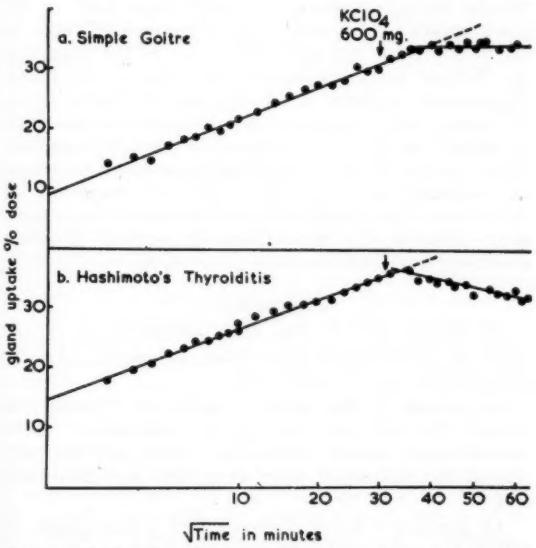

FIG. 2.—Effect of potassium perchlorate on gland uptake after intravenous injection of ^{131}I.

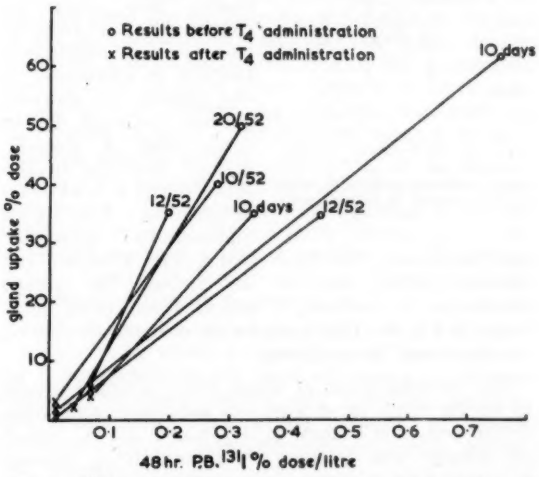

FIG. 3.—Effect of L-thyroxine sodium on the gland uptake and P.B.^{131}I. Numbers indicate duration of treatment.

uptake and basal metabolism. We have found a similar lack of correlation between the uptake and both basal metabolism and the serum cholesterol. It is clear that a number of anomalous results are to be expected when ^{131}I tests are used in the investigation of hypothyroidism. A normal thyroid uptake, or more rarely even an elevated uptake, does not eliminate the diagnosis of myxoedema. Indeed, its occurrence in a patient who presents the clinical picture of myxoedema and who has received no antithyroid drug therapy must suggest the possible diagnosis of Hashimoto's thyroiditis. In euthyroid patients with a firm goitre in whom there is a diagnostic difficulty in distinguishing between Hashimoto's thyroiditis and subacute thyroiditis, a normal uptake of ^{131}I favours the former condition and a low uptake favours the latter.

The presence of relatively high levels of serum P.B.^{131}I has been noted previously—for example, by Owen and McConahey (1956) in 13 out of 37 cases, by Doniach and Hudson (1957) in four cases, and by Beare (1958) in one case. In the present series elevated levels of P.B.^{131}I, such as are usually accepted as suggestive of thyrotoxicosis, were found in 58% of the cases. It is clear, therefore, that the P.B.^{131}I value must, especially if it is not supported by the results of other tests, be interpreted with caution and in the light of the clinical picture.

When the results of the ^{131}I uptake studies and the serum P.B.^{131}I are considered in conjunction more useful information is obtained. It is clear that unusual combinations of results, such as a low or normal uptake of ^{131}I in association with an elevated serum P.B.^{131}I, deserve careful thought, and when they are found, a diagnosis of Hashimoto's thyroiditis should always be considered. Likewise, Hashimoto's thyroiditis is a possibility when an elevated uptake of ^{131}I and a raised serum P.B.^{131}I are found in a patient who is being investigated as a likely case of myxoedema. Similar unusual combinations of results may, of course, also occur in patients who have received previous antithyroid therapy, in carcinoma of the thyroid, in sporadic goitrous cretinism, and in some cases of sporadic goitre. Scanning of the thyroid may help to differentiate between Hashimoto's thyroiditis and neoplasm. We have found, like Doniach and Hudson (1957), that in the former the isotope distribution is uniform, a typical result being illustrated in Fig. 4. This is unlike the unequal distribution usually found in carcinoma.

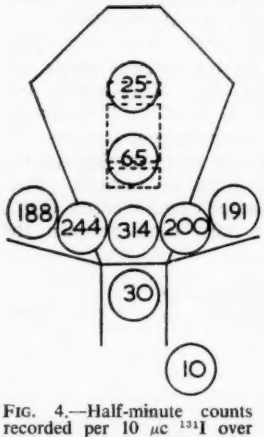

FIG. 4.—Half-minute counts recorded per 10 μc ^{131}I over neck, sternum, and heart, with G.-M. counter in contact with skin.

The elevated levels of serum P.B.^{131}I would appear to be the result of at least two different mechanisms. Owen and McConahey (1956) found in the serum of patients with Hashimoto's thyroiditis an unusual iodinated protein which, being butanol-insoluble, they considered to resemble thyroglobulin. They found that in about one-third of the patients the proportion of serum P.B.^{131}I that was butanol-insoluble exceeded the butanol-soluble P.B.^{131}I. We have also found, in three patients studied, that an appreciable proportion of the total P.B.^{131}I is butanol-insoluble—namely, 44% to 54.9%. The suggestion by Owen and McConahey (1956), that this abnormal protein might represent a leak from damaged thyroid cells, may be of significance in view of the more recent studies of auto-immunization in this condition. Nevertheless, it should be noted that in one of our patients, as in four cases described by Owen and McConahey (1956), the butanol-soluble fraction is also significantly elevated. This suggests that the high levels of P.B.^{131}I do, in part, reflect a rapid production and discharge of hormone with an unusually large number of its molecules labelled with ^{131}I because of a diminished thyroidal iodine pool (Riggs, 1952; Blom and Terpstra, 1953; Wayne, 1954).

Morgans and Trotter (1957) showed that in Hashimoto's thyroiditis there was a fairly rapid discharge of radioiodine from the gland after an oral dose of potassium perchlorate. Using a modified technique, our experience with this test has been similar. We have found it especially useful in those patients in whom the consistency of the gland suggested Hashimoto's thyroiditis but in whom routine ^{131}I tests were normal. In all of the seven patients with Hashimoto's thyroiditis there was an appreciable discharge of ^{131}I from the thyroid. Such a result demonstrates defective organic binding of iodine. This defect in hormone synthesis is only rarely encountered in untreated patients with simple goitres.

Skillern *et al.* (1956) showed that the administration of thyrotrophic hormone (T.S.H.) to patients with Hashimoto's thyroiditis failed to produce any increase in the uptake of ^{131}I. They considered that the thyroid gland was under maximal stimulation by T.S.H. We were unable to estimate the T.S.H. levels in blood or urine, so we could not make direct observations of anterior pituitary thyrotrophic activity in our patients. We therefore used thyroxine to study it indirectly. Thyroxine depresses the anterior pituitary and the output of thyrotrophic hormone falls. Reduction of thyroid activity as shown by suppression both of the gland uptake of ^{131}I and of the serum P.B.^{131}I may be taken as indirect evidence that prior to the thyroxine the thyroid has been under the influence of T.S.H. Suppression occurred in all the patients tested. It is, of course, well recognized that in thyrotoxicosis such treatment produces no change in the ^{131}I findings (Werner *et al.*, 1952). This suppression test is therefore of practical value in those patients suspected of Hashimoto's thyroiditis in whom the radioiodine studies show values in the toxic range, as a result of which confusion with thyrotoxcosis might arise.

Summary

The results of ^{131}I tests are reported in 41 proved cases of Hashimoto's thyroiditis, of which 23 were hypothyroid and 18 euthyroid.

The results of the thyroid uptake of ^{131}I and the serum P.B.^{131}I tests are often anomalous. They provide more useful information when they are considered in conjunction than when they are considered singly.

An elevated P.B.^{131}I occurred with a low uptake of ^{131}I in five cases, and with a normal uptake in 17 cases. Such a combination of results should suggest the possibility of Hashimoto's thyroiditis.

When both the serum P.B.^{131}I and the thyroid uptake of ^{131}I are raised, as in two of our cases, distinction from thyrotoxicosis may be achieved by the thyroxine suppression test.

The raised serum P.B.^{131}I may be due in part to the presence of an abnormal iodinated protein in the blood and in part to the unusually rapid production and discharge of hormone from a gland with a low iodine pool.

The observation of the effect of potassium perchlorate, which discharges an appreciable amount of the thyroid ^{131}I content in cases of Hashimoto's thyroiditis, is a useful additional diagnostic aid.

Part of this work was carried out during the tenure of an appointment by one of us (I. P. C. M.) in the Department of Medicine, Gardiner Institute, Western Infirmary, Glasgow, and we thank Professor E. J. Wayne for permission to publish the results obtained in patients who were under his care. We also thank Dr. E. G. Oastler for his helpful advice and criticism. Part of the expenses of the investigation were met by the Rankin Fund of Glasgow University. This research programme has been supported by a grant to one of us (E. M. McG.) from the Scottish Hospital Endowments Research Trust.

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The International Atomic Energy Agency has decided to undertake the measurement and analysis of samples of air, water, soil, and food to help in determining the degree of radioactivity in man's environment. This work, which will be done in the Agency's laboratory, now being built near Vienna, will be undertaken at the request of member states and of international organizations which have relations with the Agency and in collaboration with the United Nations Scientific Committee on the Effects of Atomic Radiation. Arrangements will also be made in the laboratory for a limited amount of training of scientists from interested member states in the relevant techniques. Collection of samples and their analysis would indicate the amount of radioactivity, and help in taking measures to reduce the radiation hazards of peaceful atomic energy work. Several member governments have asked the Agency how it can assist them in the collection of samples and in subsequent analysis and measurements. The Agency's assistance may also take the form of provision of experts and equipment to interested member states for carrying out measurements on the spot and helping national programmes of work in this field. It is expected that, apart from direct and specific assistance, the Agency's work will help in establishing international standards of sampling, measurement, and analysis. (International Atomic Energy Agency. PR 60/9.)

RENAL AGENESIS AND SEVERE URINARY TRACT DYSPLASIA*

A REVIEW OF 50 CASES, WITH PARTICULAR REFERENCE TO THE ASSOCIATED ANOMALIES

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Babies born with renal agenesis, and other forms of severe urinary tract dysplasia, show certain characteristic clinical and pathological features. In 50 cases encountered by us the abnormalities of the urinary tract were as follows : bilateral renal agenesis in 28, severe bilateral cystic dysplasia in 17, and congenital urethral atresia in 5 cases. The fact that intrauterine foetal micturition could not have been present was a feature common to all the cases.

Clinical Features

Quantity of Liquor Amnii

In the 50 cases reviewed the following clinical observations on liquor volume had been recorded: deficiency or absence of liquor specifically recorded in 7, notes suggestive of liquor deficiency in 28, relevant information not recorded in 14 cases, liquor present in 1 case.

The one case in which liquor was definitely present was of particular interest, the foetus being an iniencephalic with bilateral renal agenesis. The possible significance of the iniencephaly in relation to the fact that liquor was not only present but in excess is discussed later.

The following features were regarded as " suggestive " of oligohydramnios: (1) The finding at examinations in late pregnancy of a uterus smaller than expected from the duration of amenorrhoea. (2) Failure to record rupture of the membranes or escape of liquor at any time before or during labour. The space on the case sheet for the insertion of the time of rupture of the membranes was frequently left blank ; in the hourly or half-hourly labour records the membranes were often stated to be intact within 10 or 15 minutes of the time of delivery, but there was no record of their having ruptured, or having been ruptured, between this time and the delivery.

To test the reliability of these criteria a series of 100 case records of patients who were delivered of normal babies was sampled. By the above criteria, only 3 out of the 100 suggested a deficiency of liquor. The finding of these features in 28 of the 50 cases of renal dysplasia is therefore extremely significant.

Nevertheless, the most convincing cases are the first small group in which a specific record was made of the liquor deficiency. In three of these a provisional diagnosis of renal agenesis was made at antenatal examination, and the virtual absence of liquor confirmed by particular observation during labour and delivery.

*Based on a communication to the Pathological Society of Great Britain and Ireland, July, 1958.

Radiological Appearances

Antenatal radiological examination in cases of renal dysplasia usually shows signs indicative of oligohydramnios. The foetal spine appears to be collapsed on an antero-posterior picture, and is confined to the

FIG. 1.—Antero-posterior antenatal radiograph at 35 weeks. Note the extreme flexion of the foetal spine, simulating the collapse which occurs with intrauterine foetal death. There was clinical oligohydramnios, and this baby was subsequently shown to have renal agenesis.

projected outline of the pelvic brim (Fig. 1). Although the foetus is usually alive its radiographic appearance is identical with that which Tager (1952) claimed was diagnostic of foetal death *in utero*. Spalding's sign is, however, not present. Antenatal radiological films were available in seven of the cases studied: four showed extreme flexion of the foetal spine, while the remaining three showed cramped positioning of the foetal limbs with the soft-tissue outline of the uterus closely applied to the foetus.

Presentation at Delivery

The presentation of the foetus at the time of delivery was recorded as follows: breech presentation, 30 cases; vertex presentation, 19 cases; presentation unknown (caesarean section), 1 case. Thus 60% of the babies were delivered by the breech. This extremely high incidence of breech presentation cannot be explained on the grounds of prematurity, because 36 out of the 50 babies in this series were delivered after the 34th week of pregnancy.

Neonatal Survival

All of the 33 babies born alive died early in the neonatal period. The average duration of life was 3 hours 9 minutes and the longest period of survival was 36 hours. The clinical picture in these cases was always one of respiratory distress, and the cause of death appeared to be asphyxia rather than anuria. Blood chemical examinations carried out at necropsy in 6 cases showed no significant abnormality.

Intrauterine Foetal Growth

Babies born with absent or non-functioning kidneys tend to have dry skins, but the skin is also often loose and wrinkled, giving in some cases an appearance of "premature senility" (Fig. 2). In general, the babies are small for the maturity, and appear as if they had failed to gain weight or even to have lost weight.

FIG. 2.—Facies of a baby with renal agenesis. Note the low-set ears, the marked epicanthic folds, the small flattened nose, and the receding chin.

This clinical impression was confirmed by examining the birth weights of the 50 babies grouped according to maturity at the time of delivery. In Fig. 3 are shown the average weights of the babies in this series compared with those of normal babies of similar maturity. It will be seen that up to 34 weeks the abnormal babies are of approximately the expected birth weight, yet after 34 weeks they apparently failed to gain weight. The heaviest birth weight was only 5 lb. 1 oz. (2.3 kg.).

This is unlikely to be a chance finding, as 32 of the babies were delivered after 34 weeks; nor is it likely to be simply a measure of the absent organs, because (1) the weight of the kidneys is trivial compared with

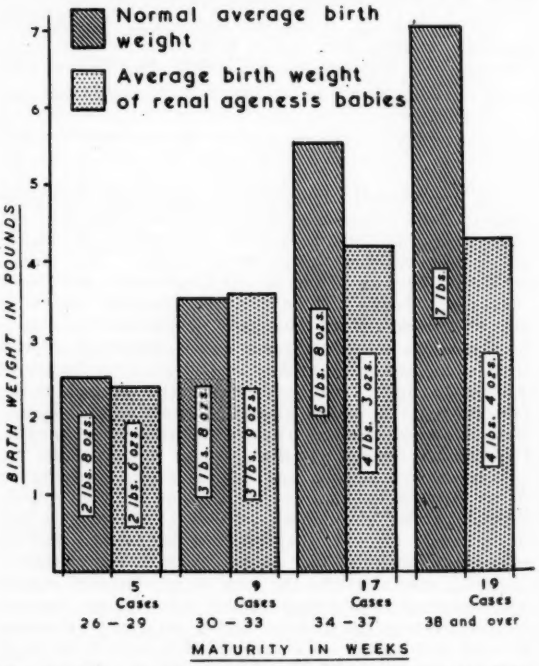

FIG. 3.—The average birth weights of babies with renal dysplasia, grouped according to maturity (stippled columns), compared with the normal average birth weight of babies of comparable maturity (obliquely hatched columns). It will be seen that the babies without kidneys fail to grow to the expected weight beyond 34 weeks' gestation.

the overall body weight; (2) 22 of the cases were of cystic dysplasia in which there would tend to be an *increased* kidney weight; and (3) it is only in *late* pregnancy that the foetal weight is less than expected.

Pathological Features

Face

The distinctive facial characteristics found in association with renal agenesis have become widely recognized through the writings of Potter (1946a, 1946b, 1952). The main features she described were abnormally large low-set auricles, prominent epicanthic folds with increased space between the eyes, slight flattening of the tip of the nose, and a conspicuous crease below the lower lip with recession of the chin. Although Potter originally described these features as associated with renal agenesis, she subsequently noted that such features could also be found with severe forms of renal dysplasia.

These features are all variable, however, and no single one is constantly present. In 10 (20%) of the present series of cases the facial changes were not definite enough to make the diagnosis prior to necropsy. Those which lacked the typical facial appearances were distributed as follows: renal agenesis, 4 cases; severe cystic dysplasia, 5 cases; urethral atresia, 1 case.

Hands

During the course of this study, one of us (A. D. B.) noted a peculiar appearance of the hands. They were broad, clumsy, and "spade-like"; not infrequently there was redundant skin on the dorsum, while the fingers were relatively short in relation to the width of the palm (Fig. 4).

Subsequent to recognition, this appearance of the hands was found to be present in 35 out of 38 consecutive cases, and it has proved to be a most valuable adjunct to the facial appearances in making a diagnosis.

Feet

The occurrence of some form of talipes was extremely frequent. Four foetuses were severely macerated and seven had gross defects involving the caudal region, such as spina bifida or sirenomelia. Excluding these, talipes in some form, either unilateral or bilateral, was present in 28 out of 39 cases—an incidence of 72%.

Lungs

Pulmonary hypoplasia is an almost constant finding in association with renal agenesis or severe cystic dysplasia. In our series it was present in all cases.

Amnion

The association of amnion nodosum with renal agenesis or severe dysplasia has been recorded elsewhere (Scott and Bain, 1958). This condition affects particularly that portion of the amnion which covers the placenta. The lesions take the form of small grey-yellow nodules of 1–2 mm. diameter which may coalesce to form plaques of larger dimensions. On cursory examination they may simulate miliary tubercles. They are found to lie on the foetal surface of the amnion and can be detached from the membrane without disrupting its continuity.

Histologically (Fig. 5) the nodules consist of masses of keratinized squames embedded in an acidophil matrix. The cuboidal cells of the amniotic epithelium are absent in the region of the nodules. There is no evidence of any squamous metaplastic change.

Since these nodules were first observed by one of us (J. S. S.) we have had the opportunity of examining 10 placentae belonging to the present series of cases. All but one of these showed amnion nodosum, the exception being the iniencephalic foetus with renal agenesis. In this, the only instance out of the whole series in which liquor amnii was definitely present, amnion nodosum was absent and there were none of the facial features associated with urinary tract dysplasia nor was there any abnormality of the hands or feet.

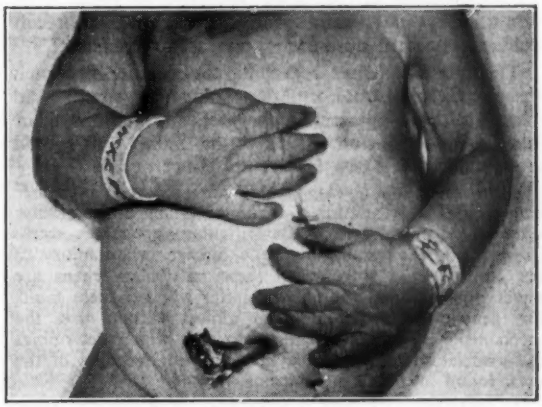

FIG. 4.—Photograph of the large, clumsy, spade-like hands of a baby with renal agenesis.

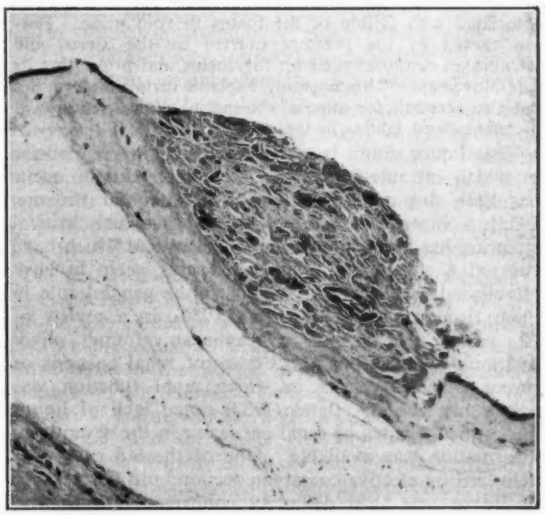

FIG. 5.—Photomicrograph of an amnion nodosum lesion showing keratinized squames embedded in an acidophil matrix. Note the break in continuity of the amniotic cells and the absence of squamous metaplasia. (H. and E. ×110.)

Discussion

The findings in this study substantially confirm Potter's observations on the facial appearances found when the foetus is incapable of micturition. These features, however, are not always present or are not always sufficiently well developed to enable a diagnosis to be made prior to necropsy.

In this series, additional features were observed in a high percentage of cases. These included broad spade-like hands and a nodular condition of the placental amnion—"amnion nodosum." Even when the facial

appearances are normal or doubtfully abnormal, attention to the changes in the hands and amnion makes diagnosis possible. Other points which can be used in corroboration include the presence of talipes, the fact that the baby is considerably under-weight, and antenatal or intranatal evidence of a deficiency of liquor amnii.

What might be termed the "ante-post-mortem" diagnosis of severe renal dysplasia is a matter of greater concern to the obstetrician than Nash (1951) suggests. The majority of these babies present by the breech, and the recognition of the signs indicative of gross renal abnormality in a baby dead or dying after breech delivery saves the obstetrician unnecessary remorse.

The question arises regarding the manner in which these congenital malformations, affecting tissues and organs with no apparent embryological, anatomical, or functional connexion, come to be linked. It would seem that at least two factors are concerned.

1. *Intrinsic: Maldevelopment of the Tissues of the Early Embryo.*—The association of maldevelopment of the urinary tract and displacement of the auricular appendages seems likely to be the result of genetic linkage or an injury to the embryo at a stage when these particular organs are undergoing differentiation. No matter whether these faults are genetic or acquired, it is almost certain that the mechanism concerned is similar to that which determines the association of gonadal dysgenesis with webbing of the neck found in Turner's syndrome.

2. *Extrinsic: Liquor Deficiency.* — Although some fundamental error in development, such as is postulated above, must be held responsible for certain defects, others are undoubtedly the result merely of the oligohydramnios associated with failure of the foetus to void urine. They are caused by the pressure exerted by the uterus and membranes firmly applied on the foetus and preventing its free movement. This not only explains certain deformities but also accounts for some of the special clinical features of pregnancy and labour in these cases.

That liquor amnii is usually deficient in pregnancies in which intrauterine foetal micturition cannot occur has been disputed in the past (Browne and Browne, 1955). Nevertheless, those papers in which critical attention has been paid to this problem and which have covered a substantial number of cases, seem to have established that oligohydramnios is the general rule in these circumstances. Bardram (1930), in a review of 20 years' material in Copenhagen, found oligohydramnios in 10 out of 13 cases of renal agenesis or severe cystic dysplasia in which renal function was apparently absent. Bates (1933) noted lack of liquor in 6 out of 7 cases of renal agenesis; in the seventh no information was available. One of these 6 cases was delivered by elective caesarean section, and the absence of liquor was thus definitely confirmed. Bates also referred to 7 cases of extreme renal hypoplasia, in all of which liquor deficiency was noted. His total figures thus present a picture of 14 cases of agenesis or severe hypoplasia with oligohydramnios recorded in 13 and no information in the fourteenth.

Potter (1952) stated that in 30 cases in which necropsy revealed renal agenesis in the foetus, liquor amnii had not been seen at the time of delivery by any obstetrician. She further commented: "Membranes are commonly thought to be intact during the course of labour because a history of rupture is lacking, but when no fluid is found at delivery the conclusion is ordinarily reached that the membranes ruptured previously with loss of fluid despite the absence of such history." This seems to have been the sequence of events in some of the cases recorded with allegedly normal liquor volume.

Hinman (1940) and Plentl and Gray (1957) stated that normal amounts of liquor "may be found" or "are frequently found" in association with a congenital foetal abnormality incompatible with micturition. They did not, however, adduce any evidence to support these statements. Perhaps the most important case recorded is that by Selby and Parmelee (1956), who saw a baby without kidneys, born with the amnion intact. No liquor was present. Recently, Weber and Israel (1958) reported two cases of renal agenesis and one of renal hypoplasia all associated with oligohydramnios.

Nevertheless, there are several cases, and the one reported here, in which liquor was without doubt present. In our own case the renal anomaly was associated with iniencephaly, the latter defect being likely to make the foetus unable to swallow. This appears to be the mechanism which leads to hydramnios in cases of anencephaly (Scott and Wilson, 1957) and will presumably also operate in cases of iniencephaly.

The mechanism of production and disposal of liquor amnii in normal pregnancy, together with the findings in cases of oligohydramnios and polyhydramnios, are reviewed elsewhere (Jeffcoate and Scott, 1959). These findings lead to the general conclusion that, if the

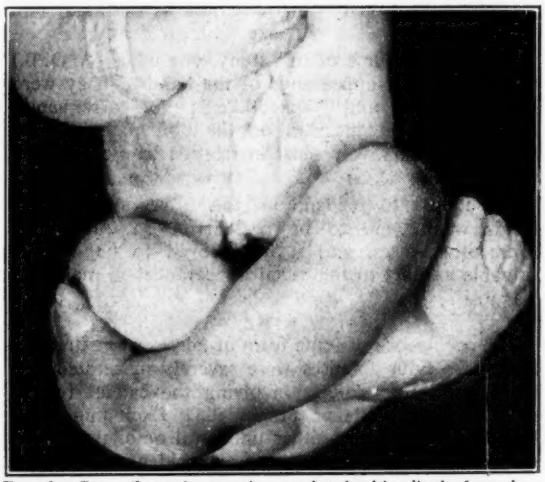

FIG. 6.—Case of renal agenesis associated with oligohydramnios and amnion nodosum. Note the position of the legs and the glazing of the skin over the external malleoli, suggestive of pressure.

mechanisms for disposal of liquor are operating normally, absence of foetal urination will be associated with oligohydramnios. In cases in which there is some interference with the normal channels of disposal, liquor which has arisen from non-renal sources may accumulate.

The effect of a deficiency of liquor shows in the radiological signs, mentioned previously and described by Kent, Rubin, and Dann (1957). The high incidence of breech presentation is almost certainly a consequence of the lack of liquor, which prevents the foetus turning in the normal way to adapt itself to the uterine shape in late pregnancy. Amnion nodosum seems to be specifically related to oligohydramnios. The only one of our cases in which this was searched for and not found was that in which liquor was present. In addition, we have observed amnion nodosum on three occasions in association with oligohydramnios not due to renal dysplasia. It appears that when the liquor

is deficient the foetal prominences rub and abrade the surface of the amnion; desquamating foetal epidermal cells then become adherent to these denuded areas, forming the nodules.

Talipes is probably another effect of oligohydramnios; indeed, in several of our cases there were skin marks suggestive of pressure on the external malleoli (Fig. 6). These findings confirm the views of Browne (1936, 1955) on the importance of intrauterine pressure in the production of deformities such as talipes. It seems possible that the flattened hands associated with renal abnormalities are also due to pressure secondary to the liquor deficiency.

The explanation of pulmonary hypoplasia is more doubtful, but this condition could be the result of oligohydramnios rather than of a genetic taint. Compression of the thoracic cage or absence of the normal volume of liquor circulating into the developing lungs might be responsible. If, however, the pulmonary abnormality is primary, it has to be recognized that it might in part be the cause of the oligohydramnios. This possibility has to be entertained because Whitehead, Windle, and Becker (1942), Macafee (1950), and Morison (1952) have suggested that the lungs contribute to the volume of liquor.

That some of the facial features, such as the low-set ears, are embryological defects seems certain, but others, such as the flattened nose-tip and the receding chin with its deep fold, may well be the effect of the dry amniotic sac being tightly applied to the foetus.

The failure of the affected foetuses to gain weight in the latter weeks of intrauterine existence remains to be explained. Three possibilities present themselves. (*a*) It may be that the foetal kidneys are normally important for excretion of the products of foetal metabolism. This is opposed to the generally accepted concept that the placenta is the essential excretory organ for the foetus *in utero*. Moreover, it is rendered unlikely by the fact that babies born devoid of renal function show no gross change in the blood levels of urea and other waste products (Davidson and Ross, 1954). (*b*) It may be that the imbibed liquor amnii normally nourishes the foetus. This is unlikely if this fluid, as found in late pregnancy, represents mainly foetal urine. (*c*) The third possibility is that foetal growth is normally dependent on progressive distension of the uterus by amniotic fluid. Adequate distension of the uterus may well be necessary for proper placental development and function.

This last explanation appears the most likely and is in agreement with the conclusions of Harrison and Malpas (1953), who, in regard to early pregnancy, concluded that the function of liquor at that stage of pregnancy is to provide a distension-growth stimulus to the uterus. They showed a definite correlation between the volume of liquor and foetal size. Textbooks have for long recorded the association of hydramnios with large babies and oligohydramnios with small babies, but it has always been assumed that the volume of liquor is secondary to the size of the foetus. The opposite cause-and-effect relationship may well obtain.

The fact that the iniencephalic foetus (maturity 30 weeks), which, despite absence of renal function, was surrounded by liquor in large amount, was the only one which failed to show any defects such as talipes, spade-like hands, amnion nodosum, and peculiar facies is strong supportive evidence for the concept that liquor deficiency is the principal mechanism of production of these features. The birth weight in this case was 2 lb. 5 oz. (1,050 g.), but if allowance is made for the considerable tissue deficiency constituting the iniencephaly the weight of the baby probably corresponded to that expected from the maturity. Further evidence that many of the external features which we have described are the effect of oligohydramnios rather than of a genetic linkage is the fact that these features were found in association with urethral atresia—an anomaly which is embryologically quite distinct from renal agenesis.

Summary

Fifty cases of severe urinary tract dysplasia are reviewed (28 of bilateral renal agenesis and 22 of other anomalies incompatible with micturition). The characteristic clinical and pathological features are described.

During the intrauterine period there often is evidence of deficiency of liquor amnii, suggesting that foetal urine provides a major contribution to liquor volume in late pregnancy. In the only case in which liquor was definitely present the foetus was also iniencephalic. The significance of this is discussed. Characteristic intrauterine radiological appearances are described.

At delivery the foetus presented by the breech in 30 of the cases. The average period of survival of the 33 babies born alive was 3 hours 9 minutes; death being apparently due to asphyxia. A comparison of the birth weights of these babies with the normal average at comparable maturity shows a failure to gain weight after the 34th week *in utero*.

The characteristic facies was present in 40 of the cases, while flattened spade-like hands and a peculiar nodular appearance of the amnion—"amnion nodosum"—were other common features. Pulmonary hypoplasia was a constant finding and is the usual cause of death. Diagnosis of these anomalies during life is usually possible, and may be of some value.

The cause of the associated anomalies is discussed. A genetic factor appears to operate, but many of the features are evidently a consequence of oligohydramnios, which is due to absence of the foetal urinary contribution to the liquor amnii. Oligohydramnios accounts for the amniotic lesions, the talipes, some of the facial features, the high incidence of breech presentation, and the radiological appearances. The impaired foetal growth in late pregnancy is also probably due to liquor deficiency, and suggests that the distensile effect of liquor amnii on the uterus is just as necessary for normal foetal development in late pregnancy as it is in early pregnancy.

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Addendum.—Since this paper was prepared we have encountered 10 further cases. In eight, liquor was noted to be deficient or absent, and in all of these amnion nodosum was present. In one case of renal cystic dysplasia associated with hydrocephalus and spina bifida, liquor volume was apparently normal and there was no amnion nodosum. The

remaining case resembled the one in the text, having both renal agenesis and iniencephaly. Again there was hydramnios and a normal amnion.

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RELATIONSHIP OF STRESS TO THE DEVELOPMENT OF SYMPTOMS IN ALOPECIA AREATA AND CHRONIC URTICARIA

BY

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Agreement has not yet been reached on the part played by emotional disturbance in the development of two common disorders, alopecia areata and chronic urticaria. In an attempt to assess the relationship of psychological stress to symptoms, a study was made of patients suffering from these two conditions in the out-patient department of St. John's Hospital for Diseases of the Skin. The effects of *adequate* psychotherapy on symptoms were also studied. The study depended on the taking of a very long and detailed history of every case (when necessary, over several interviews of an hour each), together with a careful follow-up of patients, each of whom was seen at short, regular intervals over a period varying from 3 to 18 months, during interviews which lasted from 45 to 15 minutes. Most patients were followed up for more than one year.

The time devoted to the patients seemed to be of extreme importance. Many were not able to discuss their difficulties in the first few interviews, but as time went on they were able to talk more freely. From the therapeutic point of view also, the time devoted to each patient was of major importance. In many studies of this kind the psychotherapy offered may consist of brief interviews spaced widely over a varying period. In the present study it was, in certain cases, not possible to give adequate psychotherapy for the condition, the psychological disturbance being too profound.

There were 52 cases of alopecia areata and 27 cases of chronic urticaria. The groups are here treated first separately and then together, as the conclusions relate equally to both groups. Patients were referred for psychiatric assessment in a haphazard manner by various members of the staff of St. John's Hospital. There was no definite selection of cases, but it is possible that physicians remembered to refer patients when some psychological disturbance seemed present. Cases were studied between the beginning of July, 1957, and the end of January, 1959. All the cases were followed up for three months at least, several for more than a year. In both these groups there was not a single patient who did not reveal either a very unhappy or stressful life previous to onset of alopecia or urticaria, or moderately severe neurotic symptoms in life previous to onset of symptoms. Frequently there was a combination of both.

The patients were divided into the following groups.

Group A: Those in whom a long history of stress had occurred before the onset of symptoms. Symptoms might have been precipitated by a sudden fresh stress—major in character.

Group B: Those in whom a long history of stress had occurred before the onset of symptoms. Symptoms might have been precipitated by a sudden fresh stress—minor in character.

Group C: Those in whom a long history of stress had occurred before the onset of symptoms, without a fresh, obvious stressful situation precipitating symptoms.

Group D: Those in whom no very clear history of stress was obtained, but signs of previous psychological disturbance were present—for example, insomnia, fear of crowds, fear of the dark, nervous breakdown, and so on.

Group E: Those in whom symptoms were associated with an obvious depressive illness—that is, severely depressed mood, insomnia, loss of weight, feelings of guilt, inadequacy, refusal to go out, and so on.

Group F: Those in whom the symptoms occurred in conjunction with other so-called psychosomatic illness—for example, asthma.

Group	Alopecia Cases	Urticaria Cases
A: Long history of stress and major crisis ..	6	1
B: ,, ,, ,, ,, ,, minor ,, ...	9	13
C: ,, ,, ,, ,, ,, but no crisis discovered	27	7
D: Psychological disturbance but no stress ..	4	2
E: Depressive illness (but always stress as well) ..	3	2*
F: Other psychosomatic illness	3	2

* Plus considerable stress and also crisis.

The groupings of the 52 alopecia cases and the 27 urticaria cases are shown in the Table. The urticaria patients were tested in the laboratory and not found to react to specific allergens.

Alopecia Areata

The following case-histories illustrate the type of case in the various groups.

Group A

Case 1.—The patient, aged 15, was the elder daughter in a family of two girls. Both parents are alive. The mother, a weak psychopathic woman, had had a love affair with another man (who was a minor criminal, often in trouble with the police) while her husband was away in the Forces during the war. Some time before the development of the present crisis the mother's lover turned up again. She found herself greatly attracted to him and would go out to be with him on the pretext of going to visit her mother. This was suspected by the husband and family, and tension gradually increased. One day the mother went out and took

an overdose of barbiturates. The patient, with her father and sister, waited anxiously for the mother to come home that night, not knowing what had happened to her. At midnight or later, the police arrived with the news that the mother was in a coma in a local hospital. She recovered from the barbiturate poisoning and entered a mental hospital as a voluntary patient, but she remained there only three days. During these three days a policewoman called at the house to inform the patient that her aunt, the mother's sister, had committed suicide in some town in the Midlands. The patient had to go to the funeral with her father. A day or two later the mother insisted on discharging herself from hospital and returned home. She was in a disturbed state of mind, but apparently not certifiable. The patient had to remain away from school in order to look after her mother. She experienced an intensely difficult time. She had to do the housekeeping and look after her younger sister as well. Shortly after the mother's return home, the patient's hair began to fall out in patches. She had never had a previous attack of alopecia areata, and there was no family history of this condition. The patient received support from me, and help as much as possible with out-patient psychotherapy. Her mother was interviewed and advised. The patient was encouraged to live her own life outside the home. Her hair gradually grew again.

Other examples of major crises were: (1) Accidents with cars or motor-cycles—in which the patient had committed an injury or caused death to another person or simply knocked over without injuring another person (three cases of this kind). (2) Broken love affairs and disasters at work.

Group B

Case 2.—A man aged 38 had for many years shared a flat with his elder brother, to whom he said he was devoted. On one occasion, when his brother was away from home for a few weeks, he met and married on an impulse an Arab nursing sister from the West Coast of Africa who was training in midwifery at a London hospital. This woman was naturally possessive and also sharp-tempered. On the return of the patient's brother, intense hostility broke out between her and the brother. This lasted for a year or two. After a particularly severe row the wife left the flat and her husband, and there then followed an appalling scene between the patient and his brother. A little while after the incident the patient's hair began to fall out. The situation gradually improved. The brother took a flat of his own. The wife returned to the West Coast of Africa. In the resulting atmosphere of extreme calm the patient's hair grew again. There was no previous history of alopecia areata and no family history of this condition.

Group C

Case 3.—This patient, a man aged 48, had unfortunately married an alcoholic, by whom he had one son. During her bouts of drinking the wife would go off with other men and remain away for days at a time. Finally she left with another man and did not return. During the weeks which followed her departure, both the patient and his son suffered from an attack of alopecia. The wife made trouble from time to time over the years. The patient's present attack of alopecia, which was total, including beard and eyebrows, coincided with extreme unhappiness and frustration at work. He was helped to adjust to his difficulties. His hair grew again.

Case 4.—An intelligent but very shy man of 28 had been married three years. After 18 months of marriage a son had been born. The patient's wife had had a very bad time with the birth. As a result she said she did not want any more children. Without discussing the matter with her, the patient felt that the only way to avoid further pregnancies was to refrain from sexual intercourse entirely. He said he thought this was what his wife wanted. The last year before he attended at the hospital had been a considerable strain on him, on account of his self-imposed restraint, and during this time his hair had begun to fall out in patches. He had never had a previous attack of alopecia areata, and there was no family history. As a result of psychotherapy he was able to discuss the situation with his wife, who also had been most unhappy about the matter, and intercourse was resumed. The patient's hair quite rapidly grew again.

Group D

Case 5.—A fireman aged 43 developed alopecia in a mild form. No precipitating cause could be found. For years, however, he had suffered from nightmares which would cause him to wake up screaming, and he also suffered from insomnia at times. There was no previous attack or family history.

Case 6.—This patient had tried to become a teacher in the department of adult education. He had at one time been a regular soldier. Some months after his training in adult education had begun he was told by the authorities that his temperament was unsuitable for the work, and that he was too nervous. He was advised to find another occupation.

Case 7.—This patient, a boy of 15, was the only child of a very disturbed woman who herself suffered from skin rashes and had had a nervous breakdown. The boy himself suffered from attacks of depression for no known cause and insomnia.

Group E

These three patients had very unhappy lives, but, in addition, coinciding with the onset of alopecia, they had symptoms of quite severe depressive illness—that is, mood change, self-reproach, loss of appetite and weight, insomnia, loss of interest in life, and even retardation. Their depression was, in all cases, more important and disturbing to the patients than the alopecia. As the depressive illness improved, so did the alopecia.

Group F

The three patients in this group also suffered from stress and difficulties in their environment. The additional illnesses were asthma in all three cases—one patient also had gastric ulcer and urticaria.

Urticaria

Major crisis does not seem to play a great part in precipitating chronic urticaria, at any rate in the cases studied here. Minor crisis seems, however, important.

Group A

Case A.—This patient, aged 43, was an intelligent and devoted mother of a single child, a daughter. A year or two before the onset of symptoms the daughter had married and gone to Canada. Symptoms were preceded by a violent shock—the discovery that the girl had a growth in the bone of her right femur. The fluctuations in the appearance and disappearance of this patient's rash coincided remarkably closely with the news which she received from Canada over the next few months. The unfortunate daughter went through a series of operations and courses of deep *x*-ray therapy. Whenever her symptoms grew worse my patient's rash became worse. Suddenly the patient and her husband were summoned to Canada. The daughter, riddled with secondaries from bone sarcoma, was dying. I saw this patient again a few weeks ago. She appeared in the out-patient department looking thin and pale. To my unspoken question, she nodded: "And as you can imagine," she said at once, "my rash has gone." Her rash has not returned since this time.

Group B

Case B.—A spinster aged 27, a resident school teacher, an only child, noticed with surprise that whenever she went to her parents' home for the week-end or they came to visit her she developed urticaria. Psychotherapeutic interviews uncovered a set of very disturbed relationships in the family. The patient's rash improved, and she later went to a job in Devon.

Difficulties with parents occurred fairly often among patients with chronic urticaria.

Case C.—This patient, a woman aged 23, was a devout practising Catholic married to a non-practising Catholic. She tried to make her husband accompany her to church and improve his views, as a result of which rows and scenes took place. After one such severe quarrel her urticaria first developed. She later noticed that after every disagreement she had a rash. She was helped by psychotherapy to adjust to the situation. With her increasing serenity her rash did not appear.

Group C

Case D.—An Irish woman was married to a man who insisted on going out to the pub of an evening. The patient herself was chained to the home because of their very difficult young children. Urticaria developed at times of rage and frustration. The urticaria improved with her ability to make adjustments to the situation, and also her husband's more considerate behaviour after interviews. When last seen she had had no rash for eight months, and was cheerful and well.

Group D

Case E.—An electrical engineer aged 32, a bachelor, with no friends either male or female, and no hobbies, lived at home with his parents. He was a completely passive, apathetic man, though very good at his work. He had been working for a long time at a job he did not like. He was a chronic masturbator, and as a result suffered from deep guilt. He had a daily rash. He was persuaded to find more congenial work, and generally to widen his interests. Sexual matters were discussed with him and his guilt was relieved to some extent. When last seen he had had no rash for a year, except on one occasion, very slightly, when overworked and overtired.

Groups E and F

The cases in group E were similar to those described above under alopecia areata.

The additional illnesses in group F included peptic ulcer and "nervous breakdown."

Many other examples of dramatically disturbed lives could be given.

Treatment and Progress

Treatment consisted of discussions, mainly on a superficial level, of life situations and factors causing stress. Difficulties were often obvious and florid—as described in the case histories—and concerned with human relationships. A sedative or a stimulant in the form of amylobarbitone and "drinamyl" were used for many patients, sometimes together with a small dose of barbiturate for sleeping — usually amylobarbitone sodium, 2 gr. (0.13 g.).

In the patients with alopecia areata, hair grew again completely in 35 cases; 11 were not followed long enough to know what happened to them, and six showed no improvement even after many months. These six were all cases of alopecia totalis, and had been so when first interviewed. None of these six cases was helped in any way by psychotherapy—that is, their psychological states and the circumstances in the environment could not be changed. One was a man who was impotent, married late in life to a very demanding woman who could not reconcile herself to his sexual ineffectualness. Another was a West Indian who was constantly in trouble with the police. He had killed a boy while driving dangerously in Jamaica, and had been up on a charge of manslaughter, but the jury could not agree and he was discharged. After the case he had left the West Indies and became involved in various shady businesses over here. When last seen he had had another car accident, probably while under the influence of liquor. The other four patients were equally difficult to treat.

The urticaria showed *improvement* (less frequent and less severe rash), or *great improvement* (rare, slight rash), or long *absence* of symptoms in 18 cases followed for several months or longer. Nine cases showed some improvement so long as they were followed, but the follow-up was not long enough to judge results.

Discussion

It is difficult to avoid concluding that in many of the cases described, emotional disturbance was closely related to the onset of symptoms. Whether stress was related to symptoms in all cases is doubtful and perhaps not relevant. The controversy over the relation of psychological disturbance to the appearance of symptoms has continued over many years. As regards alopecia areata, Anderson (1950), in a study of 114 cases, found that 23% had a history of mental shock or acute anxiety preceding the appearance of the bald patches. A further 22% were suffering from various forms of mental disturbance. There was, however, no correlation between persistence of the disease and the presence of mental disturbance. Irwin's (1953) series of 55 cases contained 23% in which mental trauma was considered to have caused the condition, and a further 63% classified as neurotic. Greenberg (1955) reported 44 cases, of which only 7% were free from mental illness. Recently, however, Macalpine (1958) has caried out an extensive psychiatric study of 125 selected cases, and could find no evidence that mental illness, anxiety, or mental shock plays a significant part in causing alopecia areata. One of the arguments advanced by Macalpine was that she did not find that psychotherapy could influence the alopecia areata in her series of patients, and she therefore concluded that the condition was not related to psychological stress.

As regards the aetiology of chronic urticaria, a valuable piece of research was undertaken, including a summary of a great deal of previous work on this subject, by Linford Rees (1957). He found that emotional precipitation of attacks occurred in 68% of his cases. His groups as a whole showed a statistically higher incidence of neurotic symptoms than his control group. The onset of the disorder coincided with stressful life situations in 51% of cases. Dr. Rees found no specific personality type among his cases, nor were the stressful life situations specific. Finally, the emotional precipitating factors were found to be in no way specific. Dr. Rees concluded that complex psychological and physical factors—both together or each separately—may play a part in the development of symptoms in patients suffering from chronic urticaria.

This conception of the aetiology seems to be a logical one, and one which applies to both alopecia areata and chronic urticaria—and possibly to all so-called "psychosomatic" diseases. The divergence of opinion of the various workers mentioned above surely suggests that in certain cases psychological factors predominate or are of obvious importance in the development of symptoms. In other cases, psychological factors are unimportant and physical factors significant in the development of symptoms.

The observation of Dr. Rees that there was nothing specific about the personality of the patients, or the stressful life situations, or the precipitating emotional

factors seems important to me. In the cases described above it appeared that both alopecia areata and chronic urticaria were non-specific responses to non-specific stress in persons of widely differing personality.

It is possible that patients responding with physical symptoms and psychological stress are *potentially* able to respond with the particular symptoms at the particular time. The potential response may depend upon physical disturbance of an organ, abnormal metabolism, or other factors.

In the cases described above there was no relation between intensity of stress and intensity of symptoms. What might be assessed as major stress produced in some cases slight symptoms, and vice versa.

Finally, as regards psychotherapy, it is difficult to assess its effects in the patients suffering from either alopecia areata or chronic urticaria. Both conditions are known to improve spontaneously, with or without treatment of any kind. Many of the patients treated undoubtedly benefited from the psychotherapy in that they were able to accept or alter difficult life situations and in that their anxiety or depression diminished. As mentioned above, those patients who did not improve at all were either profoundly disturbed psychologically or lived in intolerable conditions. Psychotherapy is, as yet, a clumsy and often difficult method of treatment, particularly under out-patient conditions. It is a method of treatment of immense benefit to some and hopelessly inadequate for others. It is surely unwise to come to conclusions on whether symptoms are produced by psychological disturbance or not by judging a patient's response to psychotherapy.

Summary

In an attempt to assess the role of psychological factors in the causation of the two conditions, a study was made, over a period of 19 months, of 52 patients suffering from alopecia areata and 27 patients with chronic urticaria. All patients were treated with psychotherapy for at least three months; most were treated for more than 12 months. Extensive and detailed case histories were made and patients were given long interviews for treatment. In both groups all patients were found to have either very stressful life conditions or moderately severe neurotic symptoms, or both, before the onset of the alopecia and urticaria. Examples of case histories are given. Progress and response to psychotherapy are described. It was concluded that in certain cases stress plays a part in the causation of both alopecia areata and chronic urticaria.

I thank those members of the medical staff of St. John's Hospital for Diseases of the Skin who kindly referred patients to me. I also thank the Medical Committee of St. John's Hospital for permission to use the hospital notes.

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The Minister of Health, Mr. MASON, has called for a report from the Health Department on the current shortage of house-surgeons in New Zealand hospitals. It is possible that the problem will also be examined by the committee investigating the availability and distribution of medical practitioners in New Zealand, which meets again in March. (New Zealand Release A 5/60.)

D

PITUITARY ADENOMA WITH CUSHING'S SYNDROME

BY

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Pluriglandular syndromes were described at the end of the nineteenth century. Certain disorders have since been differentiated, and in each one a single endocrine gland was incriminated as the initiator with secondary changes in the others. In 1912 Harvey Cushing described such a syndrome, which he later attributed to the presence of a basophil adenoma in the pituitary (Cushing, 1932a, 1932b). He did suggest that the adrenal glands might be the main mediators, but he thought that the original stimulus arose from the pituitary neoplasm.

In Cushing's series of cases such an adenoma was found in life only in one case, when a surgical exploration was attempted; most were discovered at necropsy (6 out of 12 cases): in none of his cases had there been any suggestion of either expansion of the pituitary fossa or chiasmatic compression.

A case is presented here in which symptoms and signs of a pituitary neoplasm preceded the development of Cushing's syndrome.

Case History

In October, 1955, a 37-year-old man presented with a four-weeks history of loss of vision. He was of average height, weighed 65 kg., and, apart from prominent eyes, his facial appearance showed no anomaly. His blood-pressure was 130/70. He had a left temporal hemianopsia and a left primary optic atrophy, with a visual acuity of 6/24 in both eyes. Skull *x*-ray films revealed a greatly expanded pituitary fossa indicative of a long-standing intrasellar tumour. This was confirmed by re-examination of a skull *x*-ray film taken in 1948 for a minor head injury, which showed a large pituitary fossa; his visual fields were full at that time.

He was admitted to hospital, and investigations showed a haemoglobin of 15 g./100 ml. and E.S.R. of 18 mm./hour (Wintrobe). C.S.F. protein was 90 mg./100 ml., with a slight excess of globulin. An electroencephalogram was normal. Skull *x*-ray films confirmed the large pituitary fossa, which obliterated the sphenoidal air sinus, the anterior clinoids were deeply undercut and the posterior clinoids eroded, while the superior orbital fissures were enlarged. Carotid arteriograms indicated elevation of both anterior cerebral arteries, left more than right. A lumbar air encephalogram confirmed that the tumour was predominantly intrasellar in site: the ventricular system was normal in size and position. The chest *x*-ray film showed nothing abnormal.

Surgical treatment was undertaken in order to prevent further loss of vision. At operation, by Mr. Leslie Oliver, a large tumour was seen in the pituitary region, displacing the right optic nerve. When this was aspirated old dark blood was obtained, and further blood and necrotic tumour tissue escaped after the capsule was incised. As much tumour as possible was removed. It was felt that the

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primary aim of the operation—namely, to relieve an optic-nerve compression—had been achieved.

During the next year he became progressively drowsy, falling asleep at any time of the day. He discovered himself to be impotent. He had returned to work as a van driver, but after four accidents it was realized that his sight was too poor, and a transfer to bench work was arranged. In September, 1958, he sustained a spontaneous fracture of his right foot. His weight increased so that in the November he weighed 92 kg. (14st. 7 lb.). It became clear that the changes in his appearance (Fig. 1) were no longer consistent with obesity alone, and a clinical diagnosis of Cushing's syndrome was made.

FIG. 1.—Photographs of patient taken in (left) 1955 and (right) 1958.

He had a red moon-face, a thick neck merging into a buffalo hump, scars of old acne vulgaris on his shoulders, and a grossly distended abdomen with purple striae in the lower half and a girth of 48 in. (122 cm.). There was wasting of the muscles of the thighs and the pectoral and pelvic girdles. He was euphoric though normally orientated in time and space. There was right-sided exophthalmos, and visual testing showed that with the left eye he could only perceive hand movements, while the acuity of the right eye was 6/18 with an upper temporal quadrantic defect. Bilateral primary optic atrophy was now present. His blood-pressure was 190/120; he had ankle oedema and dyspnoea.

Investigation showed a haemoglobin of 13.5 g./100 ml., white-cell count of 14,000/c.mm. (82% polymorphs, 18% lymphocytes, and an absolute eosinophil count of 18/c.mm.), and an E.S.R. of 4 mm./hour (Wintrobe). Urine contained no protein, sugar, or casts. A glucose-tolerance test gave a fasting level of glucose of 120 mg./100 ml., with levels at half-hourly intervals after 50 g. of glucose of 150, 200, 130, and 100 mg./100 ml. Serum electrolytes on admission were sodium 143, potassium 4.2, chloride 96.5, and alkali reserve 25.3 mEq/l. and a blood urea of 26 mg./100 ml.

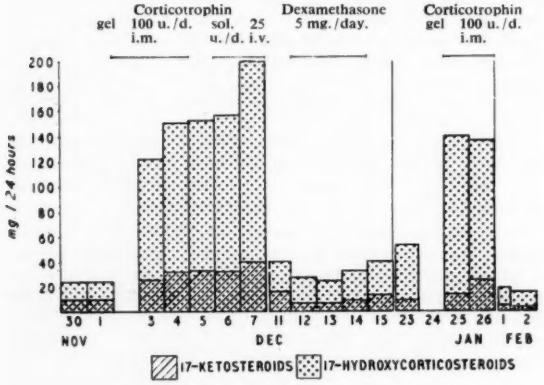

FIG. 2.—Urinary steroid output.

The urinary steroid output was measured for two control days and stimulation tests were performed, first with intramuscular corticotrophin gel (100 units daily for three days) and subsequently with intravenous corticotrophin (25 units daily by eight-hourly infusions on two consecutive days). Later a suppression test was carried out with dexamethasone (1.25 mg. six-hourly for three days). The results are shown in Fig. 2, and demonstrate an increased response to corticotrophin, and that the steroid output could be influenced by dexamethasone. Plasma corticotrophin concentration was measured by Dr. Barbara Clayton and found to be 80 international milliunits (i.m.u.) per 100 ml. (normal level is less than 1 i.m.u./100 ml.). During the stimulation test with corticotrophin the plasma potassium level fell to 2.9 mEq/l. and the alkali reserve rose to 34 mEq/l. The patient complained of muscle weakness in his thighs and buttocks. After the above tests these values returned to their normal ranges with disappearance of the symptoms. Radioisotope studies one week later showed that the total exchangeable potassium was 1,850 mEq (normal is 45 mEq/kg. of body weight). The radiographic appearance of the skull did not show any change, but there was a true increase in the size of the heart, with widening of the aortic arch. The dorsal spine showed the changes of osteoporosis, and in the right foot there was evidence of previous fractures in the second and third metatarsals. A ventriculogram showed that the floor of both anterior horns, right more than left, and also of the third ventricle, was displaced upward.

It was concluded that a recurrence of the pituitary adenoma was responsible for the clinical picture, and a further attempt at direct removal was made. Pre-operative therapy consisted of 100 mg. of cortisone acetate daily by intramuscular injection for four days. At operation on January 1, 1959, by Mr. Valentine Logue, an approach was made under general anaesthesia through the old right frontal bone flap. The tip of the right frontal lobe was amputated to give adequate exposure. A cystic tumour was found and incised; there was a gush of 3–4 ml. of a yellowish fluid. When the capsule was dissected away the tumour was seen to fill an enormous pituitary fossa, infiltrating and blocking both cavernous sinuses. All accessible tumour, apart from that around the ocular nerves and chiasm, was removed. Packs and guttapercha were used to control excessive bleeding, and the wound was closed but not sutured. Two days later the operation site was re-exposed and a dry field obtained; suture was then performed.

Post-operative therapy comprised cortisone acetate in the first three days by intramuscular injection in daily doses of 100 mg. and then by mouth in a dose of 75 mg. daily, with a gradual withdrawal over the next six weeks.

Post-operative studies showed a haemoglobin of 12.2 g./100 ml., a glucose-tolerance test with a fasting blood sugar of 75 mg./100 ml. and levels at half-hourly intervals after 50 g. of glucose of 125, 175, 160, and 120 mg./100 ml. Fig. 2 shows that the augmented response to corticotrophin was still present. Plasma corticotrophin concentration was 80 i.m.u./100 ml.

^{131}I studies before and after operation showed:

Date	24-Hour Uptake of ^{131}I
30/12/58	19%
22/1/59	Less than 6.5%
10/3/59	17%

Because it was thought that active tumour remained in his right orbit, a course of radiotherapy was given. The patient was transferred for this to Mount Vernon Hospital under the care of Dr. A. M. Jelliffe, and was treated with the linear accelerator. He received 3,528 r to the right lateral temporal region and 2,128 r to the left anterior oblique facial region. He remained well for three weeks and then developed marked ankle oedema, for which he

was treated with mersalyl and a low-salt diet. The course of radiotherapy failed to produce any improvement in his "Cushingoid" state, and after a further two weeks he became incontinent of urine and complained of further visual deterioration in his left eye. He was transferred back to the Middlesex Hospital, where he was found to be confused, dyspnoeic, and cyanosed, with a temperature of 104.6° F. (40.3° C.). There was a coarse tremor of his left hand and profound weakness in all limbs but no other neurological signs. His blood-pressure was 115/85.

Investigations showed the plasma potassium to be 2.4, sodium 156, chloride 94, and the alkali reserve over 40 mEq/l. Blood urea was 49 mg./100 ml. Urinary electrolyte levels were potassium 58, sodium 2, and chloride 7.9 mEq/l.

He was treated with ammonium chloride, oxygen, and hydrocortisone, but he collapsed, dying 12 hours later.

Post-mortem Report (Dr. R. E. Cotton)

A large irregular and partially necrotic tumour mass was centred around the expanded and distorted pituitary fossa. The tumour was 1½ in. (3.8 cm.) in diameter with little upwards projection but gross invasion of surrounding structures in the base of the skull. Serial slices through this region demonstrated extension of the tumour into the sphenoidal air sinus, both cavernous sinuses, the retro-orbital tissues through the fissures, and downwards to erode and ulcerate the roof of the nasopharynx. Much of the tumour was infected, and infection had tracked forward below the right frontal lobe, giving rise to an abscess 1 in. (2.5 cm.) in diameter in the region of the amputated tip of the frontal lobe. There was oedema and softening of the surrounding brain but no evidence of rupture into the ventricular system. The hypothalamic region of the brain showed some distortion and there was slight hydrocephalus, most pronounced in the third and right lateral ventricles.

Sections of the tumour showed infection and necrosis in an invasive adenocarcinoma of the pituitary. Much of the tumour was well differentiated and recognizable chromophobe and chromophil cells were present, though in more anaplastic areas distinguishing features were lost.

The heart weighed 17 oz. (482 g.) and showed hypertensive left ventricular hypertrophy. There was bilateral adrenal cortical hyperplasia, most pronounced in the zona fasciculata; the right adrenal gland weighed 18.8 g. and the left 20.3 g. The thyroid gland weighed 18 g. and was of normal naked-eye and microscopical appearance. The testes were normal in size, though showing slight atrophic changes in the seminiferous tubules.

Discussion

Harvey Cushing, when he first described his syndrome, suggested that it might be due to a basophil adenoma of the pituitary. Allbright (1943) emphasized the importance of disturbance of adrenal cortical function in this condition, and there now seems to be little doubt that the essential abnormality is an increased level of circulating hydrocortisone. This may come from a functioning tumour of the adrenal cortex or from hyperplasia or hyperfunction of the glands. Knowlton (1953), from a review of the literature, found that an adrenal cortical adenoma or carcinoma was present in 30% of published cases; more recent figures suggest that the proportion of cases due to neoplasm is between 10% and 15% (Nabarro, personal communication).

Overproduction of hydrocortisone by a hyperplastic adrenal cortex could result from an excess of circulating corticotrophin or from abnormal responsiveness of the adrenal cortex to normal amounts of corticotrophin. Attempts to demonstrate an excess of corticotrophin in the plasma of patients with untreated Cushing's syndrome have seldom been successful (Taylor *et al.*, 1949; Paris *et al.*, 1954). The methods available are relatively insensitive and the presence of a slight excess cannot be excluded. It has, however, been possible to show increased levels of melanophore-expanding substance (Sulman, 1952), and an adrenal growth-promoting factor (Jailer *et al.*, 1957). There is some evidence to suggest that while the adrenal glands are producing an excess of hydrocortisone they exert an inhibitory effect on the pituitary even in a patient with Cushing's syndrome.

If the condition is treated by total adrenalectomy the level of circulating hydrocortisone is reduced and increased production of corticotrophin follows. This may be detected clinically by the occurrence of pigmentation, which is known to be associated with increased secretion of corticotrophin, as, for example, in Addison's disease (Sulman, 1952; Nelson *et al.*, 1958; Rees, 1959). Total adrenalectomy for Cushing's syndrome has been followed in a number of cases by the appearance of symptoms and signs indicating the presence of a pituitary tumour. It has been suggested that while the adrenal glands are present they secrete an excess of hydrocortisone and that this inhibits the activity of the pituitary adenoma, but after total adrenalecomy and a drop in the level of circulating hydrocortisone not only does the pituitary adenoma produce more corticotrophin but also it actually grows more rapidly and so becomes clinically apparent (Salassa *et al.*, 1959).

It has therefore become necessary to re-examine the relationship of pituitary adenomata to Cushing's syndrome. Cushing found a basophil adenoma in 6 of his 12 original cases. Susman (1935) pointed out that basophil adenomata were often found in the pituitary gland at necropsy without any evidence of Cushing's syndrome. Knowlton (1953) collected 58 reports of necropsies in patients with Cushing's syndrome due to adrenal hyperplasia. She noted that 24 were found to have basophil adenomata of the pituitary, and 10 had chromophobe or mixed adenomata or carcinomata.

One point to be considered is the speed with which the two conditions—pituitary tumour and Cushing's syndrome—develop symptoms and signs. Since steroid therapy has been used for the treatment of collagen diseases it has become apparent that gross changes appear within a few months of administration of large doses; the speed of recurrence after operation in patients with secondary deposits of functioning adrenal cortical carcinoma also leaves little doubt that Cushing's syndrome is a condition that develops rapidly and is obvious clinically in many cases in a matter of months. Pituitary tumours, however, are much slower to produce clinical or radiological manifestations. Richmond (1958), in a series of 220 cases of pituitary tumour, found an average delay of seven and a half years between the onset of symptoms and the presentation to the doctor. Hence, if the syndrome were produced initially by an overfunctioning adenoma of the pituitary, symptoms and signs referable to it might not be evident at the time of presentation of the endocrine disorder.

Cases of concomitant Cushing's syndrome and chiasmatic compression are recorded by Cohen and Dible (1936), Petit-Dutaillis *et al.* (1938), Lisser (1944), Forbes (1947), McCormick *et al.* (1951), Sheldon *et al.* (1954), Bayliss (1957), and Mogensen (1957) in which chromophobe adenomata were found in five cases, basophil

carcinomata in those of Cohen and Sheldon, and an eosinophil adenoma with acromegaly in McCormick's case. All showed bilateral adrenal cortical hyperplasia.

Cases in which the symptoms and signs of pituitary tumour developed after the onset of Cushing's syndrome are reported by Glenn *et al.* (1958), Nelson *et al.* (1958), Rees (1959), and Salassa *et al.* (1959). In all these cases subtotal or total adrenalectomy had been performed prior to the appearance of chiasmatic compression. Skull *x*-ray films before adrenal surgery were thought to be normal. The pituitary tumours found were mostly chromophobe adenomata, but Salassa did find basophil adenomata as well.

The course of the present case is unusual. The presence of a pituitary abnormality was found accidentally seven years before it produced evidence of chiasmatic compression. A local invasive pituitary lesion was demonstrated surgically three years before Cushing's syndrome was diagnosed. A high level of circulating corticotrophin was found, but pigmentation was not a striking feature. Despite the high level of corticotrophin, exogenous corticotrophin produced an abnormal response by the adrenal glands. The output of corticotrophin was apparently suppressed by dexamethasone, indicating that the pituitary carcinoma was not autonomous in its activity.

Only two other cases have been found in the literature, in which it is clear that a pituitary tumour was present before Cushing's syndrome manifested itself. Messimy *et al.* (1950) describe the case of a woman of 57 ; when 28 she had had a year's amenorrhoea, obesity, and poor sight, which responded to radiotherapy to her skull ; this treatment was repeated, but in her early fifties Cushing's syndrome appeared. On presentation she had, as well as her endocrine disorder, a bitemporal hemianopsia and an eroded pituitary fossa shown by radiography. Feiring *et al.* (1953) record the case of a woman of 32 who had amenorrhoea and poor vision, and had gained 30 lb. (13.6 kg.) ; her pituitary fossa was irradiated without relief. At craniotomy a chromophobe adenoma was removed with remission of her symptoms ; she subsequently had two pregnancies, one resulting in the birth of a healthy infant. Four years later she developed Cushing's syndrome and died. Necropsy revealed an invasive pituitary carcinoma with metastasis to the anterior cranial fossa, and there was bilateral adrenal cortical hyperplasia, each gland weighing 12 g.

It seems clear that a proportion of cases of Cushing's syndrome may be started by a pituitary adenoma, which is often chromophobe and sometimes basophil in cell-type. This tumour may be clinically detectable before the syndrome develops, coincidentally with it, or after it has been successfully treated.

A careful study of the sella turcica by skull *x*-ray films and the charting of visual fields are essential in any case of Cushing's syndrome, especially in those believed to be associated with bilateral adrenal cortical hyperplasia. It is important to look for subsequent changes in these findings after adrenalectomy.

In the presence of a pituitary tumour that threatens the visual pathways a direct surgical approach to the tumour is necessary. It is problematical whether in the absence of chiasmatic compression it is still advisable to perform a hypophysectomy if the pituitary is shown to be the instigator of bilateral adrenal cortical hyperplasia. In the present case surgery was not helpful in alleviating the endocrine disorder ; post-mortem study confirmed both the failure and the impossibility of complete surgical removal, and, furthermore, showed that radiotherapy had neither halted the tumour's growth nor arrested its function.

Summary

A case is described in which the presence of a pituitary tumour was demonstrated at least seven years before the detection of Cushing's syndrome.

Investigations showed that there was a high plasma corticotrophin level, associated with a raised urinary 17-hydroxycorticosteroid output, which was further increased by parenteral corticotrophin. It was concluded that the adrenal glands were not responding maximally to the endogenous stimulus, and that in this case of bilateral adrenal hyperplasia there was still an adrenal reserve. The response to dexamethasone suggested that the pituitary tumour was not autonomous.

Surgery and radiotherapy failed to correct the course of the disease, and necropsy confirmed the presence of an invasive carcinoma of the pituitary gland.

The possible time-relations between the presentation of a pituitary tumour and of Cushing's syndrome are discussed, emphasizing that it is rare for the clinical signs of a pituitary tumour to precede those of Cushing's syndrome.

It is suggested that an active Cushing's syndrome may retard the growth of a pituitary tumour and so prevent its early detection ; but it may manifest itself after adrenalectomy.

Our thanks are due to Dr. J. D. N. Nabarro for permission to publish the above case and for his help in preparing this paper ; to Dr. Gerald Parsons-Smith, Mr. Leslie Oliver, Mr. Valentine Logue, and Dr. A. M. Jelliffe, who were at various times responsible for the patient's care and treatment ; to Dr. R. E. Cotton, who performed the necropsy ; to Dr. Barbara Clayton for the assays of plasma corticotrophin ; and to Mr. R. Neave for the figures.

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ROUTINE TONOMETRY IN 5,000 PATIENTS FOR DETECTION OF EARLY GLAUCOMA

BY

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Glaucoma, like the poor, is always with us. All ophthalmic out-patient departments have their share of tragic cases of elderly men and women with glaucoma. The incidence of glaucoma in the general population is high. In 1956 Sorsby reported that 13.6% of all blindness in England is due to glaucoma. Zeller and Christensen (1954) state that in the United States 20,000 persons are blind from glaucoma, and a further 150,000 have lost the sight in one eye. Further, a number of workers have published the results of mass survey and found that the average incidence of glaucoma in people over 40 years of age is 2% (see Table I).

TABLE I.—*Incidence of Glaucoma in the General Population Over the Age of* 40

Authors	No. Surveyed	Results
Berens and Tolman (1950) ..	10,500	2·7% ocular hypertension
Brav and Kirber (1951) ..	10,000	1·53% definite glaucoma, 0·7% borderline cases
Wolpaw and Sherman (1954) ..	12,803	2% definite glaucoma
Vaughan *et al.* (1957)	7,943	2·01% ,, ,,
Fortier (1958)	987	2·83% ,, ,,

The alert ophthalmic surgeon is always looking for minimal cupping of the disk or early field defects that will suggest the onset of this insidious disease. Primary chronic glaucoma has a point in its natural history beyond which the disease progresses to blindness whatever treatment is employed. In 1948 Kronfeld and McGarry published a five-year follow-up of more than 300 glaucomatous eyes. They found that when glaucoma was detected in an early stage and treatment was adequate, 81% showed no visual deterioration in five years, but cases discovered at a late stage showed a much poorer response to treatment.

The problem is therefore to find cases early, before damage has been done to the nerve fibres of the retina. Our colleagues who deal with pulmonary tuberculosis are faced with a similar problem and have met it by introducing mass radiography in an attempt to diagnose early cases before symptoms have developed. Have we any similar way of detecting cases of early glaucoma before visual deterioration has occurred?

Glaucoma for the most part attacks people over the age of 40. Patients in this age-group tend to consult an ophthalmologist at regular intervals because of their presbyopic needs. This provides an excellent opportunity for the screening of these patients for the presence of this disease. Detailed field studies on every patient are not practicable, but we believe there is a method of selecting those who should be subjected to further investigation. In our practice for the last four years it has been our routine to measure the intraocular pressure of every patient over 40 years of age. We have selected an arbitrary measurement of 25 mm. of mercury, and every patient whose pressure is above that figure undergoes careful investigation. Of course, we realize that this is not an infallible means of detecting glaucoma subjects, but we regard it as a practical method of screening patients for glaucoma.

Methods of Investigation

The intraocular pressure is measured by a Schiøtz or a Mueller electronic tonometer. We have trained our nurses to perform the simple test required, and in 5,000 cases we have had no complications. A drop of tetracaine (amethocaine in the U.K.) hydrochloride 0.5% is instilled into the eye. The lids are held apart by the fingers of the free hand and the instrument is rested lightly on the cornea, every care being taken to avoid all pressure on the globe. If the intraocular pressure is found to be below 25 mm. of mercury, glaucoma is assumed to be absent unless the disk appears to be cupped. If it is above 25 mm. of mercury, the patient is advised to have further investigation.

Our first step is to repeat the tonometry. If we agree that the pressure is above 25 mm. of mercury, we usually proceed to do a gonioscopy. We use an Obrig or a Goldmann goniolens. This is placed over the anaesthetized cornea, and by its means, using a hand microscope and a light with the Obrig lens, or the slit-lamp with the Goldmann lens, the corneo-scleral angle may be examined to determine whether it is of the wide or narrow type.

If the angle is narrow a mydriatic test is performed unless the pressure is significantly high. In this test the intraocular pressure is first measured, then a drop of a mydriatic solution such as homatropine hydrobromide 1%, phenylephrine hydrochloride 2.5%, or cyclopentolate hydrochloride 1% is instilled into each eye and the pressure is measured at 15-minute intervals. A rise of over 8 mm. of mercury in two hours is regarded as positive.

If the angle is wide or if the mydriatic test is negative the patient is brought back another day for a water-drinking test and for tonography. For a water-drinking test the patient attends in the morning without having had anything to eat or drink. The intraocular pressure is measured. The patient is then given a quart of water or other fluid to drink and the pressure is recorded at 15-minute intervals for one hour. A rise of 9 mm. of mercury is regarded as positive.

In cases of glaucoma there is an obstruction to the drainage of aqueous from the eye. With a tonometer it is possible to measure the degree of this obstruction and also to assess the rate of production of aqueous in the eye. This procedure is known as tonography.

We use a Mueller electronic tonometer and a Sanborn recorder. The tonometer is allowed to rest upon the eye for four minutes. The weight of the tonometer expresses aqueous from the eye and the intraocular pressure falls. This fall is recorded on a graph by the recorder and the facility of outflow of aqueous is calculated by a mathematical formula. When glaucoma is present the fall in intraocular pressure is reduced owing to the obstruction to aqueous outflow.

In practice we have tables to which we refer. From the original pressure and the fall in outflow we read off the facility of outflow and the rate of production of aqueous. We record our findings in the following way: Po—the original pressure; c—the facility of out-

flow; F—the rate of production of aqueous; P/c—the ratio between the first two. This last ratio was suggested by Becker (1956), who has shown that in a normal eye it is usually less than 100. We take 150 as indicative of glaucoma.

The visual fields are also investigated.

In some eyes the pressure as measured by the tonometer is too high or too low owing to an excess or lack of rigidity of the sclera. If an abnormal scleral rigidity is suspected it may be checked by measuring the intraocular pressure with two different weights on the tonometer. The coefficient of scleral rigidity may be obtained by referring to tables prepared by Friedenwald (1957).

Making the Diagnosis.—The criteria we use for the diagnosis of glaucoma are given below. No single indication should ever be accepted as adequate for a diagnosis of either wide- or narrow-angle glaucoma. The whole clinical picture must be considered in every case. (1) Pathological cupping of the disk. (2) Typical glaucomatous field defects. (3) An intraocular pressure of over 30 mm. of mercury on three separate occasions. (4) An intraocular pressure of over 40 mm. of mercury on any occasion. (5) A mydriatic test with a rise in pressure of 8 or more mm. of mercury. (6) A water-drinking test with a rise of 9 or more mm. of mercury. (7) Tonography with a value for the facility of outflow of less than 0.15 and with a P/c ratio of over 150.

Results

The results of our investigation are given in Table II. Routine tonometry was performed on 5,000 patients over the age of 40. On clinical grounds 43 cases were diagnosed as glaucoma (see Table III).

TABLE II.—*Results of Routine Tonometry in* 5,000 *Cases*

	No. of Cases	%
Patients selected by routine tonometry ..	217	4·3
Failed to return for investigation	82	1·6
Patients investigated	135	2·7
(a) Found to be normal	92	1·8
(b) Considered to have glaucoma ..	43	0·9

TABLE III.—*Patients* (43) *Diagnosed Clinically as Glaucomatous*

History of previous diagnosis of glaucoma ..	7
Cupping of the optic disk	15
Absolute glaucoma	5
Secondary ,, ...	11
Acute closed-angle glaucoma	2
Glaucomato-cyclitic crisis	2
Pigmentary glaucoma	1

In 217 patients the intraocular pressure was found to be above 25 mm. of mercury in one or both eyes, though no other clinical signs of glaucoma were present. These were therefore regarded as possible cases of glaucoma. Of these, 82 failed to attend for a follow-up examination. 135 patients were investigated, and 92 of these were considered to be non-glaucomatous and 43 to have the disease.

Thus glaucoma was diagnosed in 86 patients (1.7%). Since it is likely that a similar proportion of the 82 patients who did not come for further investigation would have been found to have the disease, it may be assumed that about 2% of our 5,000 patients had glaucoma.

We wish to emphasize that 43 cases of early glaucoma had no clinical signs of the disease and were discovered entirely as a result of routine tonometry. None of them gave a history of haloes, or had cupped disks. They would have been missed if tonometry had not been performed as a routine procedure.

Comment

Our finding that about 2% of patients over the age of 40 have glaucoma is in keeping with the results of similar studies which have been conducted in the United States of America and in Europe (see Table IV).

TABLE IV.—*Results of Routine Tonometry in Clinical Practice*

Authors	No. of patients	Glaucoma diagnosed before tonometry	Cases of Glaucoma which would have been missed without routine tonometry
Phelps (1949) ..	720 over 45 yrs.	2·5%	2·6%
Reed and Bendor-Samuel (1957) ..	2,000 over 40 yrs.	1·4%	1·5%
Hildreth and Becker (1957)	2,000 ,, 40 ,,	Not included	2·1%
Porter (1958) ..	2,000 ,, 40 ,,	0·85%	1·75%

Early diagnosis and adequate treatment are imperative to prevent blindness from glaucoma. We suggest that most cases can be found before damage has occurred and while treatment is of value by the routine screening of all patients over 40 years of age by tonometry. Since some might be concerned at the waste of time spent performing tonometries on the 98% without glaucoma, we would stress that our tonometries are performed by our nurses, so that no time is lost by the ophthalmologist.

We would go further and suggest that this is such a simple procedure that it should be done by every physician when conducting a routine physical examination. All patients found to have an intraocular pressure above 25 mm. of mercury should then be referred to an ophthalmologist for investigation. We realize that it may perhaps be difficult for a practising physician to make arrangements to learn a new test. It is our opinion that medical schools should seriously consider teaching this simple procedure to undergraduates as part of the normal training of a general physician.

Summary

The intraocular pressure of the eyes of 5,000 patients was measured routinely.

4.3% had a pressure in one or both eyes above 25 mm. of mercury.

1.7% were found to have glaucoma. If all those advised had attended for further investigation about 2% would have been found to have glaucoma.

0.9% of the patients were diagnosed as suffering from glaucoma on clinical examination, but 0.9% had no clinical signs of the disease and were discovered as a result of routine measurement of the intraocular pressure.

We believe that this simple test should be performed as part of the eye examination of every patient over the age of 40. It is easily performed by a nurse.

We believe that medical schools should teach undergraduates this simple test so that it is included as part of the physical examination of every patient over the age of 40.

We wish to record our thanks to our nurses, Mrs. T. Patterson, L.P.N., and Mrs. J. Proche, R.N., who have so efficiently and cheerfully performed tonometries on our patients.

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INCIDENCE OF PSYCHIATRIC ILLNESS AMONG HOSPITAL OUT-PATIENTS

AN APPLICATION OF THE CORNELL MEDICAL INDEX

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Description and Review

The "Cornell Medical Index Health Questionnaire" (C.M.I.) is a four-page self-administered inventory comprising 195 questions, which correspond closely to those usually asked in a comprehensive medical interview. There are two forms of the questionary—one for men, one for women—which are identical except for six questions in the genito-urinary section. The questions are phrased in informal language and to each the patient answers "Yes" or "No." The average time needed to complete the questionary is 10–20 minutes, and most patients find it a satisfying diversion while waiting for the doctor. The questionary is arranged into sections, as Table I shows.

TABLE I.—*Sectional Subdivision of C.M.I.*

Section	Questions Referring to	No. of Questions
A	Eyes and ears	9
B	Respiratory system	18
C	Cardiovascular system	13
D	Digestive tract	23
E	Musculo-skeletal system	8
F	Skin	7
G	Nervous system	18
H	Genito-urinary system	11
I	Fatigability	7
J	Frequency of illness	9
K	Miscellaneous diseases	15
L	Habits	6
	Mood and Feeling Patterns	
M	Inadequacy	12
N	Depression	6
O	Anxiety	9
P	Sensitivity	6
Q	Anger	9
R	Tension	9
	Total	195

The development of the C.M.I. is described by Brodman *et al.* (1949), who point out that their intention was to provide a quick and reliable method of obtaining the facts of the patient's medical history, at no expense to the physician's time. In a trial of the C.M.I. in 180 consecutive out-patients it collected most of the critical data obtained independently by the physician, and, in addition, it often gathered important material not recorded in the medical history. The patients were shown to answer the questions as accurately as they answered similar questions at interview. The C.M.I. was developed as an adjunct to, not as a substitute for, oral interview; it ensures that when the doctor sees a new patient he already has a good deal of information about him, and so is less likely to overlook important symptoms.

Brodman *et al.* (1952a) have also used the C.M.I. for evaluating emotional disturbances. They postulated that the severity of the disturbance might be susceptible of estimation either by appraisal of the responses to individual items in the questionary or by the application of scoring procedures to the data. They administered the C.M.I. to a large sample of out-patients of the New York Hospital, and found that it successfully picked out most of the patients regarded clinically as being emotionally disturbed, and was a valuable pointer to such disturbance in many other patients (Brodman *et al.*, 1952b). It was an interesting finding that, whereas physicians diagnosed emotional disturbance in their patients six times as frequently as surgeons did in theirs, scoring levels on the C.M.I. were similar for both groups.

In 1952 the *British Medical Journal* suggested that the utility of the C.M.I. in this country should be explored, particularly its ability to pick out "the anxious, the fearful, the inadequate, and the depressed." No such comprehensive investigation has yet been reported, though Leigh and Marley (1956) have used the C.M.I. to compare different groups of asthmatic patients.

The aims of the present investigation were: (1) to discover whether any relation existed between the patient's state of emotional health, and the number of positive responses to questions on the C.M.I. (2) If such relation could be demonstrated, to determine the most informative method of scoring the C.M.I. and to establish a critical score representing a boundary between "emotionally normal" and "emotionally ill," with minimum misclassification. (3) Should it prove possible thus to validate the C.M.I., to apply it to other out-patient groups with a view to assessing the amount of psychiatric disturbance among them.

Method

During an investigation into the incidence of psychiatric illness amongst out-patients attending a general non-teaching hospital (Dulwich Hospital, London), the C.M.I. was given to various groups of patients: (*a*) 100 consecutive new referrals to the medical clinics (785)*; (*b*) 100 consecutive new referrals to the surgical clinics (985)*; (*c*) 64 consecutive new referrals to the gynaecological clinics (749)*; (*d*) 50 patients who had attended the gynaecological clinics on more than six occasions; and (*e*) 30 consecutive new referrals to the physical medicine clinics (510)*.

*The figures in parentheses indicate the number of new patients seen in the particular clinic in the year of investigation.

In addition, completed questionaries were available from "normal" and "neurotic" groups. The normal group comprised 48 men and 56 women who worked at a large London store. The neurotic group included 46 men and 72 women who were attending psychiatric out-patient clinics of the Maudsley Hospital. Further details of these groups, with their total scores and scores for sections M to R on the C.M.I., are shown in Table II.

Results

Statistical comparison was made between the mean total of positive replies made by the neurotic and the normal group:

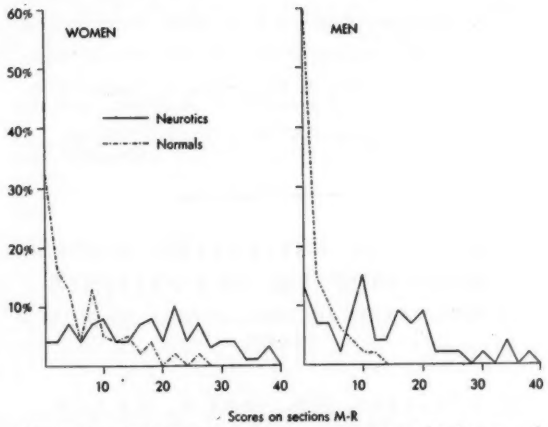
		Normal	Neurotic
Average total of positive responses	Males	11·0	32·5
	Females	20·8	45·6
For the sum of the M–R scores only	Males	2·8	14·1
	Females	6·9	18·4

These are all highly significant differences ($P>0.001$), showing that the scores could be used to separate these two groups of patients. In passing, we may remark that women tend to score higher than men and that neurotics score higher on areas A–L as well as on areas M–R. Thus the first aim of the present investigation—to discover whether the C.M.I. could discriminate between normal and emotionally disturbed patients—yielded positive results.

Our second objective—to determine a critical score representing the boundary between emotionally normal and emotionally ill—requires some elucidation. Clearly the C.M.I. does not yield perfect discrimination, but only greater or lesser proportions of misclassification. Where one draws the line depends on the purpose for which the test is used—that is, whether one is trying primarily to avoid misclassifying normals as neurotic, or neurotics as normal, or whether one is trying to reduce misclassification errors of both types to a minimum. Something also depends on the particular problem at hand, since the critical score is subject to various sampling fluctuations, and depends also on the subject's age and sex.

Brodman *et al.* (1956) suggest that "a medically significant emotional disturbance may be suspected when any of the following is evidenced on the C.M.I.: a syndrome of 'Yes' answers clinically suggestive of a psychological disorder; thirty or more 'Yes' responses in the entire C.M.I.; three or more 'Yes' responses in sections I and J; three or more 'Yes' responses on the last page of the C.M.I.†; or four or more questions not answered, answered both 'Yes' and 'No' or with changes or remarks written in by the patient." The phrase "may be suspected" clearly indicates an attempt to include all potential neurotics, at the risk of temporarily misclassifying a considerable number of normals. On the other hand, in a study of psychiatric incapacitation during Army training a critical score of 50 "Yes" responses in the entire inventory was found to yield the minimum amount of misclassification (Brodman *et al.*, 1954). Further research now in progress will throw light on the diagnostic features of each area in the C.M.I.

In the present study it was decided to concentrate on the six psychiatric areas M–R, and to try to establish first of all a critical score yielding minimum overall misclassification. The accompanying Chart shows the distribution of the M–R scores for normals and neurotics, for men and women. A score of 10 or more would yield the minimum amount of misclassification for both sexes, though clearly the precision of this discrimination leaves something to be desired. It is evident that by moving this critical score up or down one can "purify" one group at the cost of making the other group more "mixed" and increasing the total number of cases misclassified. This figure of 10 "Yes" responses differs widely from the figure of 3 "Yes" responses on areas M–R suggested by Brodman as "clinically suggestive of psychological disorder," probably because by lowering the critical score Brodman wanted to make sure that neurotic disorders would on no account be overlooked, even though quite a large proportion of normals may score between 3 and 9 "Yes" responses to areas M–R.



Distribution of M–R scores for men and women in the normal group and the neurotic group.

We may now ask what proportion of the patients in the medical, surgical, gynaecological, and physical medicine clinics showed evidence of psychiatric disturbance, as disclosed by the C.M.I. Table II shows the number of men and women in each clinic completing the C.M.I. On average, the clinic patients tended to be a few years older than the normal and the neurotic group, and this may to some extent account for the fact that the clinic cases had higher mean scores on the C.M.I. than the normal group. Mostly, however, they did not score as high as the group of neurotics. Gynaecological cases (both new and of longer standing) and those attending the physical medicine clinic tended to score a little higher than the others. While this is suggestive, it does not yet tell us what *proportion* in each clinic could be regarded as psychiatrically disturbed.

TABLE II.—*Mean Ages and Mean C.M.I. Scores of Various Groups of Out-patients*

Group	No. Completing C.M.I.		Mean Age		Mean Total Score		Mean M–R Score	
	M	F	M	F	M	F	M	F
Medical O.P.	34	61	45·2	45·6	21·4	32·4	3·9	8·6
Surgical "	26	55	49·9	42·5	20·4	31·2	3·9	9·5
Gynaecological O.P.:								
New cases	—	60	—	39·0	—	33·5	—	11·9
Old "	—	46	—	38·9	—	40·6	—	10·2
Physical medicine O.P.	10	14	49·6	49·6	36·7	33·2	9·4	11·4
Normals	48	56	36·9	34·5	11·0	20·8	2·8	6·9
Neurotics	46	72	33·9	34·9	32·5	45·6	14·1	18·4

†Areas M–R only.

TABLE III.—*C.M.I. Scores on Sections M–R for Different Groups of Out-patients*

	Medical		Surgical		Gynaecological		Physical Med.		Normals		Neurotics	
No. of cases:	M 34	F 61	M 26	F 55	New 60	Old 46	M 10	F 14	M 48	F 56	M 46	F 72
Score	%	%	%	%	%	%	%	%	%	%	%	%
0	40	14	28	7	7	14	20	7	34	9	9	1
1	18	5	20	7	7	4	—	15	24	9	4	3
2	3	3	4	9	5	2	10	7	4	14	—	—
3	9	2	15	5	5	7	—	—	6	12	8	—
4	6	7	9	5	8	2	10	7	8	4	—	4
5	—	8	—	5	3	4	—	7	6	7	2	3
6	3	7	—	5	3	7	10	—	4	5	4	4
7	—	2	—	7	5	4	—	—	4	2	—	1
8	3	8	4	4	2	4	—	7	2	2	2	3
9	3	8	4	5	3	2	10	7	—	11	4	4
10–14	3	16	16	11	15	24	10	15	8	11	25	15
15–19	9	13	—	16	15	10	10	—	—	7	15	15
20–24	3	5	—	4	12	7	20	7	—	5	15	19
25–29	—	—	—	4	2	7	—	14	—	2	4	14
30–34	—	—	—	2	5	2	—	7	—	—	2	8
35–39	—	2	—	4	3	—	—	—	—	—	4	6
40–44	—	—	—	—	—	—	—	—	—	—	2	—
10 and above	15%	36%	16%	41%	52%	50%	40%	43%	8%	25%	67%	77%
Mean score	3·9	8·6	3·9	9·5	11·9	10·2	9·4	11·4	2·8	6·9	14·1	18·4

For this we must turn to Table III. By applying the critical score of 10 to both sexes we observe the different percentages in each out-patient clinic group that could be considered to be emotionally disturbed. None of them scored as high as the neurotic groups nor as low as the normals of the same sex. Emotional disturbances were particularly frequent among the gynaecological groups, though no more so among patients of long standing than among new patients. Many physical medicine patients also scored highly, though the total number of cases was small. As before, women tended to score higher than men.

Discussion

What significance may be attached to these findings? First, let us point out that the C.M.I. is an uncommonly good discriminator, as paper-and-pencil tests go. Using the critical score of 10 and above, we have seen in Table III that only 8% of the normal men obtained such scores, against 67% of the male patients attending the Maudsley Hospital. For women, these proportions were 25% and 77% respectively. The C.M.I. score also correlated +0.56 with brief-interview psychiatric judgment, as obtained on 45 women attending a medical out-patient clinic. On the other hand, women tend to score a good deal higher than men even among the normal group, which suggests (*a*) that the test items as given have been selected with a bias towards female symptoms and complaints; or (*b*) that there is a "cultural" factor at work, which permits women to admit to a greater number of symptoms than men; or (*c*) that women on the whole really do have more emotional disturbances than men, even when they are not psychiatrically ill. Only further research can tell us which of these is the case. In addition, emotional disturbance due to the nature of the *physical* symptoms may account for some of the high scores, especially those among the gynaecological patients.

As yet the C.M.I. offers no way of distinguishing between patients who score high on sections M–R of the index because they are worried and upset by physical illness and those who are hysteric or hypochondriacal. Finally, as Table III shows, by moving the critical score different estimates of the proportion of emotionally disturbed patients would be obtained. At what point the C.M.I. evidence of emotional disturbance becomes equivalent to a diagnosis of neurosis or psychosis is difficult to say without further research. The four criterion groups of normal and neurotic men and women yielded only 20% and 24% misclassification, respectively, using a critical score of 10 and above.

Conclusions

The results of this pilot inquiry suggest clearly that the incidence of emotional disturbance among out-patients attending various clinics can be considerable. This is especially so among gynaecological patients, and also among physical medicine patients and among *women* attending surgical clinics. Psychiatric investigation of such patients would quite often seem necessary. The C.M.I. can be a most valuable instrument if used as a first diagnostic check, and further research now in progress will help to increase its usefulness and validity.

We are grateful to Dr. A. D. Leigh for completed questionaries of neurotic and normal groups; to consultants at Dulwich who allowed us to see their patients; and to Dr. Michael Shepherd, of the Institute of Psychiatry, Maudsley Hospital, who stimulated the study.

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More than 1,500 patients from the Federation of Nigeria receive treatment at Aro Hospital for Nervous Diseases each year, and the Western Nigerian Government, in whose region the hospital is located, is spending approximately £500,000 annually on the hospital's upkeep. The organization of the hospital is based on a "village system" similar to the "guild system" now operating in Belgium. Under the scheme, patients live with their relatives in surrounding villages. The recent acquisition of modern equipment is said to be yielding excellent results. (*Western Nigerian News*, WNG./132.)

PROLONGED NEUROPSYCHIATRIC DISABILITY AND CARDIOMYOPATHY IN ACUTE INTERMITTENT PORPHYRIA

BY

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Acute intermittent porphyria has not been discussed in British psychiatric reports since the articles by Hare, 1953; Olmstead, 1953. We report the case of a woman who was admitted to psychiatric institutions on six occasions with classical symptoms that were not recognized.

Case Report

A 56-year-old housewife was admitted urgently to Dulwich Hospital on April 28, 1959, complaining of having had severe generalized abdominal pain and vomiting for two weeks. Examination revealed a thin dehydrated patient with deep epigastric tenderness, who was disorientated in time and place, and whose blood-pressure was 80/60. The urine passed after admission was "port wine" in colour.

Her history revealed that she was illegitimate and had been cared for by her maternal grandparents. A second oophorectomy in 1929 cured her nine years' disabling dysmenorrhoea, the first oophorectomy a year earlier having afforded her no relief. The patient and her coloured husband insist that their marital life is happy, despite the husband's sexual promiscuity and drinking. In 1938, immediately after the death of her grandmother, the patient became depressed, lost weight, and within two months was admitted to hospital with abdominal pain and vomiting, which subsided after four weeks' treatment for peptic ulcer, despite a normal barium-meal examination. After six years of good health she had bouts of severe abdominal pain and vomiting lasting two to three weeks. Attendances at out-patient clinics were frequent, and she was variously diagnosed as a case of "functional dyspepsia" and "chronic anxiety with hysteria." In 1956 discord with her fellow tenants resulted in anxiety and depression, which necessitated her first admission to a psychiatric hospital. There was rapid improvement when new accommodation was found.

She was admitted four times as a psychiatric emergency to an observation ward in 1956–7; her reports are here summarized. *August, 1956.*—"Patient depressed, deluded, visually hallucinated; disorientation and partial amnesia." *January, 1957.*—"Patient had a history of loss of speech, blindness, and loss of use of her limbs." The incidents developed during one day and resolved in three. Examination revealed a depressed woman, aurally hallucinated. *July, 1957.*—"Admitted with depression, amnesia, and disorientation." *August, 1957.*—"Found comatose at home. Examination revealed a drowsy woman with a left wrist-drop, weakness of the left triceps, and reduction of its reflex."

In 1958 the patient was readmitted to a psychiatric hospital with a history of "blackouts." "Hyperreflexia of the left leg was present, with ataxia, which was variable and difficult to evaluate. The left triceps reflex was absent and some weakness in the left limbs was noted. A distended tympanitic abdomen was found." On each of the last four admissions a final diagnosis of reactive depression with hysterical features was made.

For the three years prior to the present admission she had been taking, initially, amylobarbitone sodium, 1 gr. (65 mg.) t.d.s., and later amylobarbitone sodium, 1½ gr. (0.1 g.) t.d.s., and pentobarbitone sodium 3–6 gr. (0.2–0.4 g.), each night.

Investigations.—The diagnosis of acute porphyria was confirmed from urinary examination by standard methods (Harrison, 1957). Second day: urine uroporphyrin 11.2 mg., coproporphyrin 230 μg., porphobilinogen 51 mg./l. After the 13th day the urine contained no detectable amounts of porphyrins or porphobilinogen. Stools (14th and 36th days): no excess of porphyrins. On admission: blood urea 50 mg./100 ml.; serum sodium 115, potassium 4.7, chloride 88, bicarbonate 26 mEq/l. After 48 hours: blood urea 35 mg./100 ml.; serum electrolytes, 123, 3.9, 96, and 25 mEq/l. respectively; these values were normal from the seventh day. Twenty-four hour urine: first day, chloride, 10 mEq/l.; eighth day sodium, 19 mEq, potassium 23 mEq, chloride 11 mEq. Corresponding values 23rd day: 57, 35, and 118 mEq/l. Serum glutamic-oxaloacetic transaminase levels: 63 units 21st day, 18 units 71st day. Repeated Hb and W.B.C., normal. E.S.R. (Wintrobe): 10 mm./hr. on admission, 34 mm. 11th day, 21 mm. 17th day. Twenty-third day: 24-hour urinary 17-ketosteroid and 17-hydroxy-corticosteroid levels 4.1 mg. and 12.9 mg., increasing to 11.3 mg. and 46.7 mg. respectively after stimulation by corticotrophin 80 units daily for three days. Urine specific gravity range, 1002 to 1030. The following investigations on serum yielded normal results: proteins, bilirubin, thymol turbidity, alkaline phosphatase, calcium, and cholesterol. Radiography of the chest (22nd and 81st days), skull, and abdomen, cholecystogram, and intravenous pyelogram were normal. Blood W.R. and Kahn test negative.

Twenty-four hours after admission her clinical state had greatly improved, the blood-pressure rose to 130/90, and she was able to take a light diet. On the third day she had two generalized fits, not clinically associated with over-hydration. No further attacks occurred after giving phenytoin sodium, 0.1 g. t.d.s. By the fourth day she was fully orientated, but she relapsed on the fifth day into a state of subacute delirium with negativism as evidenced by refusal of food. Chlorpromazine, 25 mg. t.d.s., was given, and the mental symptoms resolved during the ensuing week. Five weeks after admission she was mildly euphoric, with limited concentration and partial amnesia for recent events. A Maudsley Personality Inventory (M.P.I.) revealed the patient to be very introverted but not inside the neurotic range. Despite good physical progress, her blood-pressure on the seventh day was found to have dropped to 85/60 and there was a striking deterioration in the E.C.G. (see Fig.). Serial tracings showed gradual improvement, with a corresponding rise in the blood-pressure, and the E.C.G. was normal four months later. Chlorpromazine and phenytoin were discontinued after 10 days and replaced by chloral hydrate, 30 gr. (2 g.), for nocturnal sedation.

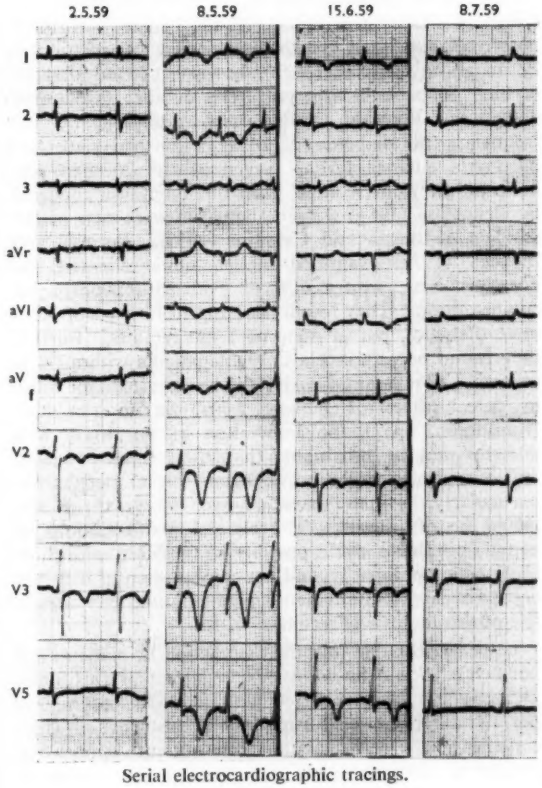
Discussion

The patient manifested at different times both depressive episodes and acute organic reactions. In addition she had a history of "blackouts," asymmetrical paresis (radial-nerve palsy), transient blindness, and "hysterical" symptoms, typical of acute porphyria. The clinical state recorded during her hospital admissions constantly revealed partial amnesia, associated with disorientation or symptoms referable to the central nervous system or abdomen. Failure to give sufficient diagnostic emphasis to the organic elements present was partly due to the adverse marital and social problems and to the improvement of her ataxia with strong suggestion. That response to suggestion is often seen in porphyria but is insufficient to warrant a diagnosis of hysteria is appreciated by Waldenström (1939). There is much to suggest that our patient's personality was unusual; this was reflected by her obsessional traits, her interracial marriage, and the

conditions of her married life. Waldenström (1939), in contrast to Roth (1945), considers porphyric patients to be "non-neurotic" between acute episodes. However, our patient was not neurotic when tested with the M.P.I., and this agrees with the findings of Luby *et al.* (1959).

In our patient two acute episodes (1938 and 1956) closely followed psychologically disturbing events. This is in agreement with the views of Eldahl (1938) and Visher and Aldrich (1954). The latter also demonstrated a rise in urinary coproporphyrin excretion of a known porphyric female after she had witnessed the death of another porphyric patient in the ward. The mental state of our patient improved concurrently with the administration of chlorpromazine (Melby *et al.*, 1956, Monaco *et al.*, 1957), though no effect on porphyrin excretion was demonstrated. Barbiturates are recognized as precipitating acute episodes of porphyria (Goldberg, 1959), and may have been of aetiological importance in some of our patient's recent symptomatology. Fluctuations in the biochemical state of porphyric patients might explain their varying vulnerability to physical or psychological factors at different episodes in their life.

Hypochloraemia and hyponatraemia commonly occur in a relapse of acute porphyria, and Abrahams *et al.* (1947) noted the resemblance to an Addisonian crisis in their patient, whose urine contained chlorides. Though Linder (1947) achieved a temporary remission with deoxycortone acetate and cortin in one case, and Goldberg (1959) claimed improvement in four cases with corticotrophin or cortisone, biochemical evidence of adrenal insufficiency was not demonstrated. Against adrenal failure in our patient were the low urinary chloride and the normal urinary steroid values.



Serial electrocardiographic tracings.

Electrocardiographic changes—commonly lowered T waves or ST segment alterations—were described by Eliaser and Kondo (1942), Halpern and Copsey (1946), Markovitz (1954), and Goldberg (1959). In the present case, the deep T-wave inversions (see Fig.) were not associated with chest pain, pathological Q waves, or injury currents. We suggest that these gross electrocardiographic alterations and the hypotension were due to a porphyric cardiomyopathy. In favour of this, Saint *et al.* (1954) demonstrated microscopically "marked disintegration of muscle fibres with loss of nuclei and striation" in a fatal case. In the present patient elevations of the erythrocyte sedimentation rate, which paralleled the electrocardiographic changes, could be regarded as further evidence of myocardial degeneration.

The present case illustrates the principle that psychological factors may precipitate physical episodes, and that symptoms responding to suggestion are not necessarily psychological. A realization of this principle, coupled with an appreciation of both physical and psychiatric symptomatology, allows a provisional diagnosis of porphyria to be made, even in the absence of the "port wine" urine. The presence of colourless porphobilinogen in the urine should, however, be confirmed biochemically.

Summary

The case reported above re-emphasizes the clinical picture of acute porphyria and the tendency to misinterpret the symptoms as hysterical. The possible precipitation of acute episodes by psychological and social factors is described.

Severe electrocardiographic changes not previously recorded in the literature are reported.

Serum electrolyte disturbances are discussed in relation to adrenal function.

We are grateful for advice and encouragement to Dr. B. J. Freedman, under whose care the patient was treated; to Dr. J. Anderson, assistant director to the Medical Unit, King's College Hospital; and to Dr. M. Shepherd, senior lecturer, Institute of Psychiatry, the Maudsley Hospital.

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PORPHYRIA CUTANEA TARDA AND DIABETES

BY

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The association of porphyria cutanea tarda with diabetes mellitus has previously been noted, and is perhaps not unusual. The case here reported illustrates the association of these conditions, and is of particular interest in that the tolbutamide prescribed for the treatment of the diabetes may have induced the clinical manifestation of the porphyria.

Case Report

The patient, a farmer aged 68, has 13 siblings, but knows of no similar condition in his family. After "shell-shock" in 1918 he developed a tremor which has persisted unchanged and for which he has taken phenobarbitone, 1 gr. (65 mg.) daily, for five years. His consumption of alcohol has been heavy for over 40 years. He has experienced no attacks of abdominal pain and no organic nervous symptoms.

In 1956, after several attacks of balanitis, he was found to have persistent glycosuria and a fasting blood-sugar of 270 mg./100 ml., and was diagnosed as a diabetic of the elderly obese type. He neglected his diet for the next 18 months, during which he felt vaguely unwell but suffered no loss of weight, polyuria, or polydipsia. In June, 1958, he was again advised to diet, and tolbutamide, 0.5 g. t.d.s., was prescribed. The glycosuria was soon controlled, and the dose was reduced to 0.5 g. b.d. and then to 0.5 g. daily.

Four weeks after he began to take tolbutamide he first noticed blisters on the backs of the hands and fingers. These appeared singly at intervals of a few days and were associated with slight burning pain. Their development was usually spontaneous, occasionally related to trauma but never to exposure to light. They were tense blisters, 1–2 cm. in diameter, sometimes haemorrhagic, arising on normal skin and healing to leave scars; they at once suggested the diagnosis of porphyria cutanea tarda.

On general examination the patient was obese and plethoric. The liver was enlarged one fingerbreadth below the costal margin and was firm. Slight gynaecomastia and palmar erythema were present but no spider telangiectasia. Body hair and pigmentation were normal. No abnormality was detected in cardiac, respiratory, or central nervous systems.

Investigations

Glucose-tolerance Test (50 g. glucose).—Blood-sugar estimations at half-hourly intervals showed 140, 193, 248, 268, 206 mg./100 ml. Glucose 1% was present in the urine at one and two hours.

Liver-function Tests.—Serum alkaline phosphatase, 4.3 Bodansky units; thymol turbidity, 3 units; thymol flocculation, nil; plasma bilirubin, 0.9 mg./100 ml.; plasma protein, 6.2 g./100 ml.; electrophoresis pattern normal.

Porphyrin Studies.—(*a*) The urine showed a slight orange coloration. No porphobilinogen could be detected with the method of Watson and Schwartz (1941). The urine, untreated and after extraction with amyl acetate, showed a strong red fluorescence in ultra-violet light, with bands at 540 Å and 575 Å. Exhaustive extraction with ether acidified with acetic acid demonstrated the fluorescence of uroporphyrins in the residual fluid phase (Varley, 1954). (*b*) A filtered 20% suspension of faeces in 10% acetic acid gave a strong red fluorescence in ultra-violet light. (*c*) Serum: no red or pink fluorescence was seen in ultra-violet light.

Progress

While the patient was in hospital the alcohol and barbiturate were stopped. After one week there was no decrease in the porphyrinuria, as shown by comparison spectroscopically with a standard solution of quinine, and one new blister appeared. He was then placed on a controlled low-carbohydrate diet and the tolbutamide was stopped. After 48 hours there was a detectable decrease in the ultra-violet fluorescence of the urine, and this continued up to the patient's discharge four days later.

For the past eight months the diabetes has been controlled by diet alone, and no further blisters have developed, though he has resumed the consumption of alcohol. Further examination of the urine showed a raised uroporphyrin (880 μg./day—normal 5–30 μg.), but normal coproporphyrin (34 μg./day) and no porphobilinogen. The faeces showed a rise in the coproporphyrins (158 μg./g. dry weight—normal 0–20 μg.) and in the total protoporphyrin (42 μg./g. dry weight—normal 0–30 μg.).

Comment

The biochemical investigations were incomplete, but the findings were typical of the cutanea tarda type of hepatic porphyria. Porphobilinogen characteristic of the acute and so-called mixed types is absent in cases without abdominal or neurological symptoms (Waldenström, 1957).

The association of porphyria and diabetes has been recognized for some years. Sterling, Silver, and Ricketts (1949) found diabetes in three out of eight patients with acute porphyria. Freedman (1956), in reporting a case of diabetes with the "mixed" form of porphyria, suggested that the association was fortuitous. Berman and Bielický (1956), however, found that 15 of their 36 patients with porphyria cutanea tarda were diabetics. Berman (1956) drew attention to the frequency of diabetes in other published cases of porphyria cutanea tarda. Seven of the 26 men, but none of the eight women, with this condition reported by Brunsting (1954) were diabetic, as were two of the patients of Borda and Campins (1950). Berman and Bielický (1956) examined diabetic-clinic clientele for porphyrinuria and for clinical evidence of porphyria cutanea tarda. They found the latter in 13 (1%) of 1,250 male diabetics, but in none of 1,430 females. Further they found porphyrinuria in eight patients without skin lesions. As examination of the urine alone may fail to detect cases of hepatic porphyria in remission (Rimington, 1952), the association of porphyria with diabetes may be still higher than these figures suggest, and a routine search for abnormal faecal porphyrins, particularly in male diabetics over 40 years of age, would be of interest. The clinical manifestations of hepatic porphyria could possibly be confused with those of diabetic neuropathy, and the combination of diabetes, hepatomegaly, and cutaneous pigmentation may suggest haemochromatosis (Freedman, 1956).

It seems probable that the association of diabetes and porphyria should no longer be regarded as fortuitous. Diabetes has been reported with all forms of hepatic porphyria—that is, using Waldenström's (1957) classification, with acute intermittent porphyria, porphyria cutanea tarda hereditaria, and porphyria

cutanea tarda symptomatica. It has been most frequently reported with the last, whence the great predominance of males. Clinical or biochemical evidence of porphyria has usually followed the diagnosis of the diabetes by several years, but has occasionally preceded it (Berman and Bielický, 1956). There would seem to be no evidence that the conditions are genetically linked. The nature of their biochemical relationship is still a matter for speculation.

The drugs most commonly implicated in the provocation of porphyria are alcohol, barbiturates, and sulphonamides. Circumstantial evidence, in particular the decrease in the ultra-violet fluorescence of the urine only after the tolbutamide was stopped, suggests that this drug may have been responsible in our patient, though it would be unreasonable to place the responsibility on the tolbutamide alone in a patient regularly consuming alcohol and barbiturates.

Summary

A case is reported of porphyria in association with diabetes mellitus.

The possibility that the clinical manifestation of porphyria cutanea tarda was induced by tolbutamide is considered.

The association between porphyria and diabetes is discussed.

We are indebted to the late Dr. N. Lawrie for the biochemical investigations.

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Medical Memoranda

Onchocerciasis Presenting without Dermatitis

It is well known that a patient from tropical Africa complaining of an irritating skin rash requires investigation for onchocerciasis, but it is not generally known that the presenting symptom may be a swollen limb in the absence of skin rash or irritation. The swelling is diffuse and firm, like a Calabar swelling, and may involve the limb completely or in part. Dubois and Forro (1939) observed non-pitting oedema of the lower leg in association with other signs of onchocerciasis, and Chartres (1955) described swelling of the upper limb as part of a reaction to the treatment of onchocerciasis with diethylcarbamazine, but the following case histories indicate that swelling of a limb may be the first clinical manifestation of infection with *Onchocerca volvulus*.

CASE REPORTS

Case 1.—An Englishman aged 37, who had spent 15 years in Uganda, returned to Britain on leave in April, 1953. The following month he developed pain in the right shoulder and a diffuse swelling of his right hand and forearm. The pain and swelling persisted. Two months later the swelling increased, and he observed that the right shoulder was also swollen. There was no skin rash or irritation. One month later (August, 1953) the swelling began to subside and had disappeared by the time he reported at the Hospital for Tropical Diseases at the end of August. No clinical abnormalities were detected, and routine tests for filariasis were as follows: Day and night blood, no microfilariae found; white-cell count, 15,300/c.mm. (eosinophils 60%); filarial skin test, positive; filarial complement-fixation test (C.F.T.), strongly positive; skin shavings, scanty embryos of *O. volvulus* found.

Case 2.—An Englishwoman aged 31, who had spent six years in Uganda, finally left Africa in March, 1956. Six months later she noticed aching pain in her right shoulder, and two months later the shoulder became swollen. Swelling and pain persisted, the pain being aggravated by lying on the right side, by exercise, and by carrying anything heavy in the right hand. After exercise such as tennis the swelling of the right shoulder increased temporarily and involved the upper arm. Dermatitis and pruritus were absent. She was seen at the Hospital for Tropical Diseases in April, 1959, two and a half years after the onset of her symptoms, and was found to have a diffuse swelling of her shoulder, which was firm, non-pitting, and of normal skin colour, resembling a Calabar swelling. The skin appeared normal. Investigations: day and night blood, no microfilariae found; white-cell count, 7,600/c.mm. (eosinophils 18%); filarial C.F.T., weakly positive; numerous embryos of *O. volvulus* found in skin shavings from the right shoulder but absent from other sites; on *x*-ray examination of right shoulder, the joint appeared normal.

COMMENT

In both patients the swelling was localized to the right upper limb, lasting for three months and two and a half years respectively, and the diagnosis of onchocerciasis was confirmed by demonstrating embryos of *O. volvulus* in skin shavings. Loiasis cannot be excluded on the grounds of absence of microfilariae of *Loa loa* in the day blood, but this finding, taken in conjunction with the fact that both patients had lived in Uganda, one of the regions of tropical Africa in which loiasis is not endemic, almost certainly excludes loiasis. In addition, a Calabar swelling usually disappears in a few days, but even when it remains for a longer period it is very unlikely to persist for three months or more. Bancroftian filariasis can be excluded by the absence of microfilariae of *Wuchereria bancrofti* in the night blood, and by the fact that the oedema cleared up spontaneously in one patient and involved the proximal, not the distal, part of the limb in the other patient; furthermore, there was no history of lymphangitis and no enlarged lymph nodes were palpated.

My thanks are due to Sir George McRobert and Professor A. W. Woodruff for permission to publish these cases.

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Reviews

THE GROUP APPROACH TO MEDICINE

Medical Surveys and Clinical Trials. Some Methods and Applications of Group Research in Medicine. Edited by L. J. Witts, C.B.E., M.A., M.D., Sc.D., F.R.C.P. (Pp. 328+ x. 35s.) London, New York, Toronto: Oxford University Press. 1959.

It seems so obvious that medical knowledge can be advanced by the use of quite different methods and skills —and, indeed, is likely to be most efficiently and rapidly advanced thereby—that one hesitates to put forward so platitudinous a thought. Yet hardly a day goes by, and rarely a weekly journal, without the statistical approach being disparaged or dismissed contemptuously by those who do not think or work that way but are highly skilled in some other discipline. Yet the many various ways of conducting research, including the statistical, constantly interact with one another and can together give a wider solution to a problem than any one of them can alone provide. Thus the astute clinical observation detects the influence of rubella in early pregnancy but cannot determine the magnitude of the risks; the designed statistical survey that provides that measure nevertheless returns the answer to the clinician to weigh in dealing with the characteristics of the individual patient. Again, the laboratory worker produces a vaccine, and almost invariably group methods must be used in the world at large to establish its value, and the prophylactic trial may indicate whereby the product falls short and needs improvement, and thus return the next stage to the laboratory. The controlled clinical trial is designed to measure the relative merits of different treatments, and one of its fundamental requirements is the clinician's precise observation and judgment of his patients. There is no reason why this approach should be detrimental, either within or alongside itself, to the observational skills we so freely attribute to our clinical ancestors. And the broad answer from the trial again goes back to the aid of the doctor faced with the individual patient. The epidemiological inquiry into the characteristics of the group will sometimes bear upon the diagnosis in the individual—e.g., the occupation of the sick person suspected of having Weil's disease. In short, there is no dearth of opportunities for the study of disease in *groups* as well as in *individuals*, and no dearth of opportunities for *both* to contribute to clinical research.

The aim of Professor Witts and his collaborators in this book has been to introduce the concepts and methods of the group approach, through medical surveys and clinical trials, to postgraduate workers in medicine. They have done so partly by precept (nine chapters on methods) and partly by example (nine chapters on selected applications). Under the former heading N. T. J. Bailey and Witts himself lead off with a discussion of the general principles and methods; the special problems of diagnosis in group research (observer error and variation) and of making prevalence surveys are then taken up by C. M. Fletcher and P. D. Oldham, who are followed by a discussion by Richard Doll of the pros and cons of retrospective and prospective inquiries. Follow-up studies and therapeutic trials are in the hands of S. C. Truelove, while J. Knowelden takes charge of prophylactic trials. Some special problems in clinical trials—volunteers, controls, placebos, and questionaries —are discussed by E. M. Glaser and operational research by Bailey. All this is simply and helpfully done, and the careful reader will learn a great deal from it about the strength and weaknesses of different ways of conducting research of this kind, from the initial consideration of his problem to the selection of controls, the appropriate form of record, and the analysis of the answers. The illustrations of the second half of the book are very varied, for they deal with genetics (A. C. Allison), nutriture (H. M. Sinclair), child development and health (Alice Stewart and Roy Acheson), chest diseases (C. M. Fletcher and A. Springett), cardiovascular diseases (B. Bronte-Stewart and G. W. Pickering), diseases of the joints (J. S. Lawrence), mental illness (G. M. Carstairs), cancer (Richard Doll), and tropical diseases (A. W. Woodruff). The editor assures us that he has taken pains to "preserve the idiosyncratic flavour" of these contributions, and there is certainly no doubt that he has succeeded. Nevertheless, they all make interesting, instructive, and sometimes provocative reading.

Towards the end of the book Professor Woodruff points out that "all research consists primarily of asking questions, secondly of devising means to answer them, and thirdly of carrying out the work required to answer them." The book itself should play a valuable part in educating clinical workers in the processes in the particular field of work with which it is concerned. Lastly, on a personal note, Professor Witts suggests that the advance of statistical techniques into clinical medicine was "hastened by the therapeutic revolution which began with the introduction of the sulphonamide drugs in 1935" and powerfully influenced "by the publication of Bradford Hill's *Principles of Medical Statistics* in 1937." Unfortunately, experience has shown that both are liable to abuse (in all senses of the word), and that both when incautiously used can produce toxic side-effects. May this excellent book escape those dangers!

A. BRADFORD HILL.

THE SAGA OF D.D.T.

D.D.T. The Insecticide Dichlorodiphenyltrichloroethane and its Significance. Volume II. *Human and Veterinary Medicine.* Edited by S. W. Simmons. (Pp. 570; illustrated. Sw. fr. 66.) Basel, Stuttgart: Birkhäuser Verlag. 1959.

The production and use of D.D.T. as an insecticide have provided an important milestone in world medical history. This book commemorates this fact and at the same time provides the reader with an extremely well documented account of the story it tells. The first 247 pages contain a critical review (with 685 references) of the action of D.D.T. upon mammals, including man. The exact mode of action of D.D.T. as a poison remains a mystery to Dr. Hayes as to others. He wisely refrains from speculation, but instead treats the reader to a well-digested account of the experimental work designed to try to discover this. While there is a reference to its effects on domestic animals and wild life, the highlight is a chapter on the toxicity of D.D.T. to man. It is refreshing to read this well-balanced account by someone who has himself made so many excellent contributions to this topic. Though no authentic cases of poisoning from occupational exposure to D.D.T. have been described, there are several good accounts of uncomplicated D.D.T. poisoning resulting from accidental ingestion in food. There are also a

great many reports of what Dr. Hayes calls "disease alleged to be poisoning." Pages 137–140 should be compulsory reading for anyone about to write an account of poisoning by any chemical when well-recognized signs of intoxication by that chemical were not evident. In the case of D.D.T. an ignorance of available information clearly has not deterred some people from attributing all sorts of illness to its effects.

D.D.T. must be unique among chemicals in having saved so much life and health at so little cost in health to those who have used it on such a tremendous scale. Some idea of this scale is given by Dr. Simmons in the next 250 pages, supported by a further 650 references. Half this section deals with malaria, and the story it tells, backed by facts and figures, must be a constant source of encouragement to public-health workers. Other vector-borne diseases are briefly discussed, but the story of typhus, particularly the outbreak in Italy during the war, is well recounted. It is often stated that D.D.T. first showed its value when used to control typhus in Naples in 1943. The lesson of this episode was that the disease could be controlled by killing the lice through personal disinfestation. The insecticides actually used were based on pyrethrum and derris, though later D.D.T. was extensively used in typhus control.

The author ends on a note of caution with a brief account of the development of insect resistance to insecticides. This underlines the need for good general hygiene in any disease-control programme. The final section of 60 pages is an illustrated summary of the insect infestations of domestic animals in the U.S.A., with brief references to D.D.T. The author is handicapped because the book is about D.D.T., whereas his subject requires a discussion of the use of many different types of insecticide.

The book is well produced, and the many references include the title of the work referred to. If there are misprints they escaped my eye, though a reference to the British Medical Society represents an uncommon synonym for the B.M.A. There is no index to this volume.

J. M. BARNES.

THE WASTE PROBLEM

The Wastes of Civilization. By J. C. Wylie. (Pp. 160. 16s.) London: Faber and Faber. 1959.

This book takes us back to fundamentals. Its theme is that by adopting the cheapest methods of disposing of sewage and household refuse we are taking a very short-sighted view, because we are failing to put back into the soil what we have taken from it. As a result the soil is becoming impoverished, and we spend millions of pounds every year on chemical fertilizers in a vain attempt to restore its fertility.

The author in his 10 chapters deals with the matter historically, starting with the Mayas of Central America, who "fell because their cities drew to themselves the fertility of their land and destroyed it." This is contrasted with the Chinese, who have farmed for 40 centuries and kept their waste products for manuring their land. It is stated that "nature requires three hundred to a thousand years to build up one inch of top-soil," and that this inch can be cleared away overnight by heavy rain or a tornado. "A country's soil once ruined cannot easily be brought back to productiveness." The text is written in vigorous, but rarely exaggerated, language, though it would have been helpful to give an exact reference for some, at least, of the more controversial statements.

The author condemns outright the urban communities who burn their household refuse and discharge their sewage into the sea, and says that the value of all the materials thrown out of British homes reaches £20m. yearly. He commends Bradford, which recovers grease from its sewage and sells it. The two main wastes, household refuse and sewage, must be considered together and used instead of being thrown away, and he advocates a composting system such as the "Dano bio-stabilizer" which is being used in Edinburgh. He affirms, somewhat optimistically, that "there will be no problem of disposing of the compost produced." In practice, however, many of the local authorities have found that transportation costs from large cities make it impossible to sell even good compost in any quantity at a price which farmers will pay. Any danger to health which might arise if these proposals were adopted, is discounted by the author on the grounds that the temperature in a compost heap is high and that antibiotics are derived from soil organisms.

It is a thought-provoking book, and every city engineer faced with the never-ending problem of waste disposal will hope that what is here advocated may some day become really practicable.

ALLEN DALEY.

SPIDERS

Vascular Spiders and Related Lesions of the Skin. By William Bennett Bean, M.D. (Pp. 372+xix; illustrated. 63s.) Oxford: Blackwell Scientific Publications. 1958.

This work is an account of many common and uncommon vascular lesions seen in the skin and observed with enthusiasm and useful purpose by the author in the course of 20 years' clinic practice. As the arresting title implies, his interest was first stimulated by his study of spider naevi. He describes their various patterns and physiological significance. Their association with cirrhosis of the liver was noted by Erasmus Wilson, though Bateman had described the lesions in 1824. A relationship with pregnancy was reported by Corbett in 1914: they appear in the second or third month, are more common in white than in coloured women, and may sometimes appear in the infant. Palmar erythema, which may accompany such spiders, the author relates to glomus bodies and arteriovenous shunts. From these features he passes to flushing, the vascular complications of carcinoid, pellagra, Cushing's syndrome, and Osler's disease among other uncommon disorders.

The book is very readable and entertaining. There are more than 900 references. The illustrations are mostly in black-and-white and could be improved, but many will delight to have this work in the library.

J. T. INGRAM.

HOMAGE TO KRETSCHMER

Mehrdimensionale Diagnostik und Therapie. Festschrift zum 70 Geburtstag von Ernst Kretschmer. (Pp. 308+vii; illustrated. DM. 36.) Stuttgart: Georg Thieme Verlag. 1958.

This large and well-produced volume of 45 psychiatric articles is written mainly in German by authors from Germany, Austria, and Switzerland. It makes pleasant and interesting reading, though many contributions are occasional and none of the papers contributes anything new to the ideas which German psychiatry has offered

before. Many fields mentioned or influenced by Kretschmer are represented in these papers apart from the multi-dimensional method of diagnosis and therapy celebrated in the title, and the book shows the many-sidedness and fruitfulness of his scientific activities. Relatively little is to be found about his remarkable discoveries and untiring work on physique and temperament, which has been largely confirmed by other methods in America, and found general recognition. A number of the papers deal with psychopathological problems, drawn mainly from Kretschmer's "Medical Psychology," in which the authors try to deepen and enlarge his views. His broad-minded approach to psychiatry shows itself in the great variety of subjects presented to him for his seventieth birthday: these include contributions alive with the peculiar romanticism of young German psychiatrists and their philosophical juggling with words, serious articles on cerebral pathology, neuroradiology, and neuropharmacology, complete with tables and factual material; and smaller, more personal contributions addressed to Kretschmer the man, with his human interest in patients and their lives.

Altogether, though none of the papers in this volume is of great scientific weight, the book is a testimony to the stimulating effect Kretschmer had on the work of other people, and to the number and devotion of the master's friends and followers.

W. MAYER-GROSS.

HUMAN AND ANIMAL MALFORMATIONS

Die Morphologie der Missbildungen des Menschen und der Tiere. Founded by Ernst Schwalbe. Edited by Professor Dr. Georg B. Gruber. Volume III. *Die Einzelmissbildungen.* Part XIX. *Missbildungen der Extremitäten.* (Pp. 683–1,004; illustrated. DM. 31.60.) Jena: VEB Gustav Fischer Verlag. 1958.

It is good to see Schwalbe's monumental volumes on malformations in man and in animals in a new edition which not only brings up to date the morphological literature but incorporates the extensive new work on the genesis of congenital defects, and the considerable genetic literature of recent years. The work is apparently being brought out in sections as they become available, and the present section of 322 pages contains full discussions of abnormalities affecting the limbs. Different chapters deal with hyperdactyly, syndactyly, lobster hand and foot, congenital synostosis, club-foot, and the less common affections. The chapter of 44 pages on lobster hand and foot and the 100 or so references to it are typical of the thoroughness of this publication. This volume is a welcome supplement to the studies in the *Treasury of Human Inheritance.*

ARNOLD SORSBY.

The ninth edition of the late Professor A. J. Clark's *Applied Pharmacology* has been prepared by Andrew Wilson and H. O. Schild (J. and A. Churchill, Ltd.; 750+xii pp.; 50s.). Most of the chapters have been rewritten, and new chapters on the pharmacology of tuberculosis and on psychopharmacology have been added. The illustrations have also been overhauled and 65 new figures added. The aim of the book is to provide the undergraduate and postgraduate student with a background of knowledge on pharmacology and its therapeutic application.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

The Foot and Ankle. Their Injuries, Diseases, Deformities, and Disabilities. By Philip Lewin, M.D., F.A.C.S., F.I.C.S. Special drawings by Harold Laufman, M.D., F.A.C.S. Fourth edition. (Pp. 612; illustrated. £5 5s.) London: Henry Kimpton. 1959.

Pressure Group Politics. The Case of the British Medical Association. By Harry Eckstein. (Pp. 168. 16s.) London: George Allen and Unwin, Ltd. 1960.

Teaching Comprehensive Medical Care. A Psychological Study of a Change in Medical Education. By Kenneth R. Hammond and Fred Kern, jun., M.D., with Wayman J. Crow, John H. Githens, M.D., Byron Groesbeck, John W. Gyr, and Lyle H. Saunders. (Pp. 642+xxii; illustrated. 80s.) Cambridge, Mass.: Harvard University Press (Commonwealth Fund). London: Oxford University Press. 1959.

Leukocyte Antigens and Antibodies. By Roy L. Walford, M.D. (Pp. 182+ix; illustrated. $6.75.) New York and London: Grune and Stratton. 1960.

Psychiatric Services and Architecture. By A. Baker, R. Llewelyn Davies, and P. Sivadon. (Pp. 59; illustrated. 3s. 6d.) Geneva: World Health Organization. London: H.M. Stationery Office. 1959.

Pigmentfleckenpolypose. Klinische, Histologische und Erbbiologische Studien am Sogenannten Peutz-Syndrom. By Dr. G. F. Klostermann. (Pp. 108+viii; illustrated. DM. 19.50.) Stuttgart: Georg Thieme Verlag. 1960.

Intérêt Clinique du pH et du MétabolismeHydro-électrolytique. By H. Jaccottet. (Pp. 48; illustrated. Sw. fr. 7.) Basle, New York: S. Karger. 1959.

Cold Spring Harbor Symposia on Quantitative Biology. Volume XXIV. ***Genetics and Twentieth Century Darwinism.*** (Pp. 321+xv; illustrated $8.) Cold Spring Harbor, N.Y.: Biological Laboratory. 1959.

Francis Bacon. The First Statesman of Science. By J. G. Crowther. (Pp. 362+xv; illustrated. 35s.) London: Cresset Press. 1960.

The Health Services of Ireland. By Brendan Hensey, B.Comm., Dip.Pub.Adm.(N.U.I.). (Pp. 168. 15s.) Dublin: Institute of Public Administration. 1959.

Progress in Medical Virology. Volume 2. Edited by E. Berger and J. L. Melnick, with eight contributors. (Pp. 234+vi; illustrated. Sw. fr. 40.) Basle, New York: S. Karger. 1959.

The Surgical Treatment of Scoliosis. By Louis A. Goldstein, M.D., F.A.C.S. Appendix: ***Anesthesia in Scoliosis.*** By Vernon Thomas, M.B., F.F.A.R.C.S. (116+xi; illustrated. 54s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

The Royal Edinburgh Hospital for Sick Children 1860-1960. By Douglas Guthrie, with various contributors. (Pp. 75+xii; illustrated. 17s. 6d.) Edinburgh and London: E. and S. Livingstone, Ltd. 1960.

The Treatment of Bronchial Neoplasms. By Robert R. Shaw, M.D., and Donald L. Paulson, M.D. With a chapter on ***Bronchial Adenoma*** by John Lester Kee, jun., M.D. (Pp. 135+xv; illustrated. 64s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Toxine et Antitoxine Diphtériques. Étude Immunologique. By Edgar H. Relyveld. (Pp. 168; illustrated. NF. 24.) Paris: Hermann. 1959.

Health and Happiness in Old Age. By Celia Westropp, D.M., M.R.C.P., and Moyra Williams, D.Phil., B.Litt. (Pp. 133. 8s. 6d.) London: Methuen and Co., Ltd. 1960.

Conservation de la Vie par le Froid. By Louis Rey. Preface by Jean Rostand. (Pp. 167; illustrated. NF. 27.) Paris: Hermann. 1959.

Modern Treatment Yearbook 1960. A Yearbook of Diagnosis and Treatment for the General Practitioner. Edited by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S. 26th edition. (Pp. 310+x; illustrated. 33s.) London: Baillière, Tindall and Cox, Ltd., for the Medical Press. 1960.

Vitamin B12. By E. Lester Smith, D.Sc., F.R.S. (Pp. 196+xii; illustrated 15s.) London: Methuen and Co., Ltd. New York: John Wiley and Sons, Inc. 1960.

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ANKYLOSING SPONDYLITIS AND UROGENITAL INFECTION

In 1926, some 28 years after the publication of his original paper[1] on ankylosing spondylitis, Pierre Marie is reported[2] to have revised his opinion on the cause of this condition to the belief that gonorrhoea played a considerable part in its development. Three years later, J. W. Visher,[3] examining 500 young ex-Service patients, found chronic prostatic infection in 87. Thirty-six of these patients were *x*-rayed, and 20 (55%) had evidence of "osteo-arthritis" in the spine or sacro-iliac joints. Because few showed affected peripheral joints, he preferred a theory of direct lymphatic spread of prostatic infection to that of blood-borne dissemination. In the years which followed, the relationship between gonococcal and non-gonococcal urogenital infection and arthritis of the sacro-iliac joints was explored in some 40 or more papers, but as many authors denied as confirmed the existence of such a relationship. Often their opinions were based on uncontrolled series, short periods of observation, biased selection of cases, and confusion between lesions of different aetiology. At that time gonorrhoea was commoner and more persistent than it is now, while comparatively few venereologists recognized the importance of non-gonococcal infection and the possibility of its co-existence with gonorrhoea.

Since the last war the development of serological tests for rheumatoid arthritis, and a clearer understanding of the natural history[4 5 6] and clinical and radiological features[7 8] of ankylosing spondylitis, have strengthened the European belief in the separate identity of this disease; while advances in the management of gonorrhoea have permitted a truer assessment of the intractable nature and alarming incidence of non-gonococcal urogenital infections. In this context it is worth while reviewing some of the more recent evidence of an association between urogenital infection and ankylosing spondylitis.

R. Romanus[9] found signs of chronic prostato-vesiculitis in 102 out of 114 cases of ankylosing spondylitis, but his otherwise convincing evidence was marred by the absence of a control group examined by the same methods. Published figures of the incidence of prostatitis in healthy males vary between 17% and 38%,[3 10–13] but these figures are of limited value because of variations in the criteria adopted in making the diagnosis. J. K. Oates[14] reviewed the limitations of accepted tests for the presence of prostatitis and described the advantages of examining five consecutive portions of freshly expressed prostatic fluid under the microscope with dark-field illumination. R. D. Catterall[15] and Oates,[16] both using this "five slide" method, published figures of 16.7%, and 20% and 25% respectively, for the incidence of prostatitis in their three groups of control subjects. R. M. Mason and colleagues,[17] using this same technique, found that 83% of 54 males with ankylosing spondylitis had evidence of chronic prostatitis, while the incidence in 85 cases of rheumatoid arthritis was 33%, a highly significant difference. These same workers brought this relationship closer by showing that the incidence of prostatitis in the ankylosing-spondylitis group followed the age distribution of the group, and did not relate to increasing age as it is known to do in normal subjects.

Further evidence is available from recent studies of similar and related disorders. Reiter's disease, in which the association with urogenital infection is now

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undoubted, has been shown by many workers to result in bilateral sacro-iliitis,[18-21] the likelihood of the involvement of these joints being proportional to the number and duration of the attacks[22] and to the severity of the initial attack.[23] Furthermore, J. Marche,[18] D. K. Ford,[24] Romanus,[25] J. Sharp,[26] and G. W. Csonka[27] have each reported the development of the full picture of ankylosing spondylitis as a late sequel of Reiter's disease, though it appears that such an event is uncommon. Catterall,[28] basing an investigation on the frequency with which iritis is associated with sacro-iliac disease, found 33 cases of Reiter's disease and 18 of ankylosing spondylitis among a group of 105 cases of non-granulomatous anterior uveitis; all showed evidence of chronic prostatic infection. D. J. Abramson and S. Kamberg[29] and also M. S. Abel[30] found a high proportion of their cases of paraplegia had developed sacro-iliitis, and the former authors reported calcification of the paraspinal ligaments in two of their more severely affected patients. The high incidence of urinary-tract infections in paraplegics is notorious, and the prostate and seminal vesicles are frequently attacked in such cases. The occurrence of both sacro-iliitis and fully developed ankylosing spondylitis has also been reported in cases of idiopathic ulcerative colitis,[31-33] but here the relationship with prostato-vesiculitis is less clear. Simultaneous infection in the lower intestine and the lower genito-urinary tract is common if not invariable in the dysenteric form of Reiter's disease,[34-36] and H. B. Jensen[37] considers that spread of infection from the pelvic intestine via lymphatics to the lower genito-urinary tract is an important cause of trouble, but the state of the rectal mucosa in ulcerative colitis usually prohibits the investigation for the presence of prostatic infection.

Such findings as these go far to prove that the relationship between chronic urogenital infection and ankylosing spondylitis is a true one, but they cannot be taken to have established an aetiological connexion. Romanus was none the less impressed with the latter possibility, adducing as further evidence of cause his finding that urogenital infection had preceded or coincided with the onset of joint symptoms in a majority of his patients,[38] and that in 37 cases exacerbations of urogenital infection had been paralleled by exacerbations of arthritis.[39] He suggested that prostato-vesicular infection spread to the sacro-iliac region via lymphatics and the vertebral venous system of Batson,[40] and postulated that arthritis developed only in those with a familial predisposition. Mason[41] was also convinced that the relationship was a true one, but pointed out that there was still no evidence of an aetiological connexion. He suggested that genetic transmission might be the more important factor. A less cogent argument has been advanced against urogenital infection as a cause on the grounds that ankylosing spondylitis begins before puberty in some 10% of cases.[4] Sexual immaturity does not protect against non-venereal urinary-tract infections, Reiter's disease,[42,43] or prostatitis,[44] and even gonorrhoea in children, though uncommon, is not a great rarity.

Progress beyond the stage of establishing this relationship is likely to be slow. Mason[41] suggests that the next step should be controlled studies to determine if treatment of prostatitis can prevent the later onset of arthritis, but there are great difficulties in a prospective study of this nature. A. J. King,[45] who initiated many of the investigations referred to here, considers that much of the problem hinges on the nature of non-gonococcal urogenital infections in general. The cause of the commonest variety, abacterial urethritis, is still unknown, and in those varieties of non-gonococcal urethritis in which an organism is regularly found proof of pathogenicity is still lacking. In ankylosing spondylitis not even the most elementary facts are known about the cause or transmission of the associated urogenital infection. Is it unique, or is it identical with abacterial urethritis? Is it a direct cause, a contributory cause, or the result of an infective arthritis? Is it identical with the infection in Reiter's disease, with the possibility that the predominant type of arthritis is determined genetically?[16]

Advances in this field are urgently needed, and the problem merits a concerted programme of investigation by bacteriologist, rheumatologist, venereologist, and ophthalmologist. It is a problem the importance of which cannot be overestimated, for its solution might well open the way to a proper understanding of a widespread communicable disease, a serious eye disease, and perhaps the chronic rheumatic diseases as a whole.

EMOTIONAL STRESS AND CORONARY DISEASE

The concept that emotional stress might contribute to the development of coronary heart disease is at present regarded with suspicion and misgiving. This is probably due to a natural desire to avoid discussing something which is not defined and is ill-understood. Perhaps the main difficulty is that emotional stress cannot be measured or compared in different communities. The degree of mental stress suffered in any given situation depends on the

individual emotional response, and what is undoubtedly stressful to some is of no consequence to others. W. Melville Arnott[1] has commented that "the life of a physician in Birmingham is surely much less stressful than that of a peasant in the Yangtse Valley, with the ever-present menace of flood, famine, pestilence, and war; or of the tribesman in Equatorial Africa tortured by the taboo and sanction of primitive belief. . . ." But is this so? People are apt to be fatalists about matters over which they have little control, and it seems possible that with prolonged exposure to apparently stressful circumstances much of the emotional response is lost. At any rate, owing to the difficulty of comparing the effects of chronic stress in one community or occupation with those in another, it may be better at present to concentrate on more acutely stressful situations capable of measurement.

Acute stress can provoke an acute emotional response. Sudden difficult and responsible decisions, short periods of intense mental activity, and unexpected domestic and financial insecurity may give rise to phases of excitement and anxiety. These episodes of severe mental duress are often limited in time, and they and their physiological consequences may be capable of definition and measurement. Acute emotional stress could contribute to the development of the clinical features of coronary disease, both by an immediate effect in increasing heart rate and cardiac output in patients with advanced coronary atheroma, and by a delayed effect in accelerating the atheromatous process.

Recently H. I. Russek[2] has shown that in 91 of 100 patients under 40 years old who developed coronary heart disease severe emotional strain preceded the attack. Though in general this is probably an overestimate, many physicians will agree that in young patients particularly the features of coronary disease often develop during or after a period of unusual occupational, financial, or domestic anxiety. Patients frequently admit to exhaustion and inability to cope with their responsibilities during the weeks or months before the onset of symptoms. The "coronary personality" has been well documented,[3] and Russek[4] found that his young coronary patients, who had an intense desire for recognition, were compulsive about time, over-scrupulous, and blind to their own limits. These men were of their own volition grossly overworked, restless during their leisure, and felt guilty when relaxing. It is probable that such men, who need and enjoy responsibility, are exposed more than others to challenging situations and react more violently to them.

Attempts have been made to measure objectively some effects of acute emotional stress. M. Friedman, R. H. Rosenman, and V. Carroll[5] studied certain results of variation in the pressure of work on accountants responsible for tax returns. During the phases of greatest pressure, when these men had to work long hours in order to submit tax returns within a limited time, the serum cholesterol rose and the whole-blood clotting-time was accelerated. In contrast the serum cholesterol was lower at times of least activity, when whole-blood clotting-time was normal. These changes were believed to be independent of variations in weight, diet, and physical activity. The same investigators[6] have recently reported a similar contrast between men who have an intense and sustained desire for achievement, who are continually in competition with others and working against time, and men who are unambitious and in less exacting occupations. An increase in serum cholesterol has also been reported to accompany the mental and emotional stress of examination week in male medical students,[7–9] but in these studies there was no control or appraisal of changes in diet or physical activity. In Russia, A. L. Myasnikov[10] has shown that stimulants of the central nervous system raise, and sedatives lower, serum-cholesterol levels. Acute emotional stress has also been shown to shorten whole-blood clotting-time and to increase blood viscosity.[11] These results may be partly mediated through augmented secretion of adrenaline and partly through increased adreno-cortical activity. The incidence of vascular thrombosis is known to be increased during administration of cortisone,[12] and the *in vitro* administration of 17-hydroxycorticoids accelerates whole-blood clotting-time and increases prothrombin consumption.[13] Since there is accumulating evidence that hormonal factors can influence both the circulating lipids and blood coagulation, it is probably through the endocrine system that acute stress produces these effects. These observations are interesting, but it is important to remember that the aetiological significance of raised serum-cholesterol

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levels and of changes shown by *in vitro* coagulation tests is still not known.

The relation between acute emotional stress and the development of coronary heart disease is worth further investigation. The development of atheroma is probably an episodic process, and may be a response to episodic events in the environment. Acute emotional stress can often be defined and some of its results measured. The recent preliminary studies of its effect on serum cholesterol and whole-blood clotting-time must be repeated and elaborated to include other aspects of lipid metabolism, blood coagulation, and fibrinolysis; the results stimulate conjecture but their real significance remains obscure. Moreover, the inheritance of the behaviour patterns, reviewed by Russek, needs further examination, and a prospective study of the incidence of coronary heart disease in certain personality types is indicated. Coronary heart disease often runs in families,[14] and, while this may to some extent be due to the inheritance of predisposing conditions such as hypertension, diabetes, and hypercholesterolaemia, each person's emotional reaction is probably partly genetically determined. Do the parents, siblings, and children of patients with coronary heart disease undertake more responsibilities than others? The effect should also be measured of acute emotional stress on arteriolar tone, on coronary blood flow and on myocardial oxygen-extraction rates. Thoughts about the stress of life in general must not distract us from studying objectively the relationship of acute emotional stress to coronary heart disease.

CARCINOGENS IN TOBACCO SMOKE

Chemical studies of tobacco smoke during the last six years have shown with varying precision the presence of a number of compounds known to be carcinogenic when tested biologically. Recent chemical and biological studies by E. L. Wynder and D. Hoffman[1 2] have given more precise qualitative and quantitative evidence of the presence of these compounds and have added to their number.

Sixteen carcinogens with varying potency have up to now been reported in tobacco smoke; they are, arsenic, 1 : 2-benzanthracene, 3 : 4-benzfluoranthene, 10 : 11-benzfluoranthene, 11 : 12-benzfluoranthene, 1 : 12-benzperylene, 1 : 2-benzpyrene, 3 : 4-benzpyrene, chrysene, 5 : 6-cyclopento-1 : 2-benzanthracene, 6 : 7-cyclopenteno-1 : 2-benzanthracene, 1 : 2-5 : 6-dibenzanthracene, 3 : 4-8 : 9-dibenzpyrene, 3 : 4-9 : 10-dibenzpyrene, 3-methylpyrene (or another alkyl pyrene), and 2-naphthol. Purely qualitative detection of constituents of tobacco smoke has always been recognized as limited in value, and so the recent quantitative experiments of Wynder and his colleagues and other investigators are worthy of special consideration.

These workers have shown that most of the carcinogenic activity of tobacco smoke as demonstrated by mouse-skin painting experiments is to be found in the neutral fraction of the smoke and especially in that fraction containing the polycyclic aromatic hydrocarbons. Individual testing of pure compounds indicates that of the polycyclic aromatic hydrocarbons present 3 : 4 benzpyrene, 3 : 4-benzfluoranthene, 10 : 11-benzfluoranthene, 1 : 2-5 : 6-dibenzanthracene, and 3 : 4-9 : 10-dibenzpyrene are the most active biologically. The quantities of these compounds measured by physico-chemical processes in tobacco smoke are very small and insufficient to account for the carcinogenic action of the whole smoke. But by using 3 : 4-benzpyrene labelled with radio-carbon (^{14}C) Wynder and Hoffman have shown that their analytical processes involving two stages of chromatography on silica gel and four stages on acetylated paper lead to a loss of about 40%, and they suggest that similar errors probably occur in their determinations of other compounds of the same class. Even this correction does not account for the biological activity of the whole smoke. Consequently, if the carcinogens when mixed are additive in their effect, there must be other compounds with co-carcinogenic or promotive properties in the smoke. A promoting effect has in fact been detected.[3] Alternatively, there may be an augmenting effect when the carcinogens are present together. Wynder and Hoffman are therefore continuing their experiments by using pure carcinogenic compounds mixed together in varying amounts, and they also propose to explore the known promoting or co-carcinogenic effect of tobacco smoke. Finally, a triumph of painstaking investigation is the isolation of 3 : 4-benzpyrene in a pure crystalline state from the smoke of 3,200 cigarettes and the reporting of its melting point and mixed melting point correct to 0.5° C.

This in brief is the present experimental position. Whether it is legitimate to extrapolate the results from mouse-skin experiments to human lung-tissue is a matter that has been debated before and admirably summarized in a recent article in this journal.[4]

The incidence of lung cancer continues to rise and the statistical relationship between it and smoking is now established without doubt. It seems unlikely that the smoking habit will diminish greatly by the voluntary action of smokers, and restrictive legislation is considered to be undesirable at present. There remains another approach to the solution of this problem—namely, attempting to reduce the amounts of carcinogenic materials in smoke. This has been shown to be a formidable task,[5] but work is being directed to this end.

[1] Wynder, E. L., and Hoffman, D., *Cancer*, 1959, **12**, 1079.
[2] —— —— ibid., 1959, **12**, 1194.
[3] —— and Wright, G., ibid., 1957, **10**, 255.
[4] —— *Brit. med. J.*, 1959, **1**, 317.
[5] Gilbert, J. A. S., and Lindsey, A. J., *Brit. J. Cancer*, 1957, **11**, 398.

KYASANUR FOREST DISEASE

In 1957 reports of heavy mortality amongst wild monkeys associated with an epidemic affecting 10% of the people in certain villages in the Kyasanur Forest in the Shimoga district of Mysore State, India, prompted an investigation in which the causative agent was identified as a virus.[1] Since its first appearance there have been two epidemics in which some 650 human cases have been reported.[2 3] The onset of the disease occurs suddenly some 3 to 8 days after visiting the forest, and is characterized by headache, fever, prostration, and severe pain in the neck, back, and limbs. Conjunctival inflammation is marked, and in some patients there is a papular or vesicular eruption on the soft palate which is not tender and may be haemorrhagic. Vomiting and diarrhoea often follow within a few days, and haemorrhage from gums, nose, lungs, or intestine may be so severe as to cause death during the second week of the disease. The central nervous system is very rarely involved. Fever usually lasts 1 to 2 weeks, and recovery is slow.

The clinical diagnosis is supported by marked leucopenia and thrombocytopenia, and by the presence of albumin, granular casts, and red blood cells in the urine. The virus is present in the blood and cerebrospinal fluid from two days before the onset of fever until during the second week,[4] and it is easily isolated by intracerebral inoculation of mice. A specific diagnosis is made by demonstrating antibodies in the convalescent serum or at an earlier stage by isolation and identification of the virus by complement fixation using standard immune serum. The virus is now known to be one of the Group B arthropod-borne viruses and to be closely related to Russian spring–summer encephalitis ; it resembles a haemorrhagic fever such as Omsk fever rather than an encephalitis.

The vector is believed to be the tick *Haemaphysalis spinigera*, and from this species numerous strains of the virus have been isolated. Human infection occurs seasonally in spring and summer (January to July), but virus has been recovered from man, monkey, or tick in almost every month of the year. Serological studies show that rodents (*Rattus* and *Funambulus* spp.) often have specific antibodies to this virus, and also some wild birds in the affected area, but not outside it.

In the 1956–7 epidemic the disease was most prevalent in young adult males engaged in forest occupations, and mortality was about 10%. There were fewer cases in the 1958 epidemic, though the sex difference was not so marked and the age-spread wider ; the mortality dropped to 3%. There was some spread of infection to adjacent areas at an early stage of the second outbreak, but the area in which transmission occurs has altered little.

One of the most interesting features of the investigation is the conclusion that the virus had not existed in the area until introduced in 1955–6. It had then spread rapidly to cover an area of about 100 square miles (250 square km.) in which it caused this new and fatal disease of man and monkeys. The infection appears now to be permanently established in the area, and it may spread from there by means of infected rodents and possibly birds.

[1] Work, T. H., and Trapido, H., *Ind. J. med. Sci.*, 1957, **11**, 341.
[2] —— —— Narasimha Murthy, D. P., Laxmana Rao, R., Bhatt, P. N., and Kulkarni, K. G., ibid., 1957, **11**, 619.
[3] —— *J. Ind. med. Ass.*, 1958, **31**, 111.
[4] —— Roderiguez, F. R., and Bhatt, P. N., *Amer. J. publ. Hlth*, 1959, **49**, 869.

CERVICAL RIB

A rib arising from the seventh cervical vertebra often produces no symptoms or signs, and a person may pass his allotted life span unaware of it. But sometimes a cervical rib causes clinical abnormalities which vary in severity from slight discomfort in the forearm to massive gangrene of the whole hand. Most of them are due to the vascular complications of this skeletal abnormality, a subject on which Sir James Paterson Ross recently addressed the American Surgical Association.[1]

At one time it was thought that these vascular symptoms were due either to irritation of the sympathetic nerve supply to the hand as it passes over the rib, or to intermittent obstruction of the subclavian artery as it passes between the end of the cervical rib and the clavicle. The investigations of Sir Thomas Lewis and G. W. (now Sir George) Pickering[2] and many others since have clearly shown that the vascular complications of cervical ribs are usually due to arterial embolism. The chain of events is that the subclavian artery becomes narrowed as it passes over the anterior end of the cervical rib ; distal to this constriction a post-stenotic dilatation forms ; and either within this dilated arterial segment, or on the wall of the artery where it has been narrowed, the blood clots. Portions of these mural thromboses may become detached and produce emboli. These emboli usually obstruct a major vessel such as the brachial artery at its bifurcation. K. C. Eden[3] in 1939 noted that vascular complications occurred only when the cervical rib was complete.

Patients with a cervical rib usually have a major vascular occlusion as the cause of their vascular symptoms.[1] In some the collateral circulation is so good that an adequate pulse can be felt in the radial artery at the wrist ; in others this pulse cannot be palpated. Most of these patients complain of pain in the forearm, sometimes spreading proximally to the whole arm ; it is felt on exercise and is relieved by rest. The pain is produced more quickly if the limb is exercised when raised. There is no doubt that this is an ischaemic muscle pain comparable to intermittent claudication in the leg. These patients also may have noticed that the hand is cold and that it becomes unusually pale when raised and blue when hung down. Sometimes they may notice numbness of the fingers and trophic changes, with ulceration ; rarely gangrene of the fingers or whole hand may develop. In these patients with severe ischaemia the radial and brachial pulses are usually absent, and an arteriogram

[1] Ross, J. P., *Ann. Surg.*, 1959, **150**, 340.
[2] Lewis, T., and Pickering, G. W., *Clin. Sci.*, 1934, **1**, 327.
[3] Eden, K. C., *Brit. J. Surg.*, 1939, **27**, 111.

may show a complete occlusion of the whole length of the brachial artery. A useful clinical finding is that the distal part of the subclavian artery may be dilated, and auscultation with a stethoscope reveals a systolic murmur at this point.

The treatment is surgical and consists in removal of the cervical rib together with the bony prominence on the first rib. At the same time it is wise to perform a sympathetic denervation of the upper limb.

GALACTOSAEMIA

Although fortunately rare, the importance of galactosaemia lies in the fact that early recognition and treatment will determine the difference between death or severe disability and a healthy infant. Workers at the National Institutes of Health in the United States[1] have established that the defect in galactosaemia is a block in the enzyme system responsible for the conversion of galactose to glucose. The affected infant is therefore intolerant of milk, and it is presumably the accumulation of galactose in the tissues, particularly the liver, brain, and lens, which leads to their damage. The established disease is characterized by failure to thrive, jaundice, and intercurrent infections, and, if death does not ensue, by the subsequent development of cataracts and mental deficiency. Evidence is accumulating to show that the relationship between inability to metabolize galactose and the production of symptoms is not a simple one. Thus healthy relatives of affected infants may give abnormal responses to galactose-tolerance tests, and previously unsuspected galactosaemia has been detected in some mentally defective children.[2] Furthermore, spontaneous "recovery" may occur in later life, though the underlying enzyme defect persists.

Clinical recognition of the established disease should not present difficulties, especially if the urine is examined for albumin, amino-acids, and reducing substances. The latter can be shown to be galactose by chemical methods or, better, by chromatography. The galactose-tolerance test gives abnormal results but is not without danger in that it may provoke hypoglycaemic convulsions. A more refined test is based on the accumulation of galactose-1-phosphate in red blood cells incubated in a medium containing galactose,[3] and it is also possible to assay the specific enzyme, phospho-galactose uridyl transferase, absence of which gives rise to the condition.[4] A simple screening test which could be applied to a large group of infants at birth would be of great value in determining the incidence of galactosaemia. The basis of treatment is the complete exclusion of lactose from the diet. In some cases it may be possible to replace milk by substances which contain small amounts of lactose, but when the infant is severely affected lactose-free diets are essential. Malt and soya mixtures fulfil this requirement but tend to cause diarrhoea, and another suggested diet was poorly tolerated by the infant described by N. L. Jones and D. Leak.[5] These authors eventually devised a suitable diet. Other varieties of milk-free cereal have been used, but some contain small quantities of lactose. It is as well to remember also that drugs may contain lactose as a base, a point of some importance if antibiotics have to be given. This is the case for both penicillin and tetracycline suspensions.

[1] National Institutes of Health, *Ann. intern. Med.*, 1957, **46**, 773.
[2] Bergren, W. R., Donnell, G., and Kalckar, H. M., *Lancet*, 1958, **1**, 267.
[3] Schwarz, V., Holzel, A., and Komrower, G. M., ibid., 1958, **1**, 24.
[4] Kalckar, H. M., Anderson, E. P., and Isselbacher, K. J., *Biochim. biophys. Acta*, 1956, **20**, 262.
[5] Jones, N. L., and Leak, D., *Arch. Dis. Childh.*, 1959, **34**, 307.

A MENSTRUAL HORMONE?

The idea that menstrual blood is something more than ordinary blood must be very old, and it is widely supposed to contain substances of which the body must rid itself. The first serious scientific work on "menstrual toxin" is probably that of O. W. Smith,[1 2] though comparatively little attention has been paid to her views. It is therefore of some interest that recent work, based on sound and accepted pharmacological principles, has shown the presence in human endometrium of slowly acting plain-muscle stimulants, and has provided evidence that these or similar substances not only appear in menstrual blood but also circulate in the systemic blood during menstruation.[3–5]

The active agents are lipids whose pharmacological behaviour is such that they can be said not to be acetylcholine, histamine, or 5-hydroxytryptamine. They are probably long-chain fatty acids. V. R. Pickles[6] has studied the myometrial responses to extracts of menstrual fluid and has found that human myometrial strips and the guinea-pig uterus are stimulated *in vitro*, while intravenous or intracardiac injections in the guinea-pig cause uterine contractions *in vivo*. It is noteworthy that the response of human myometrial strips may consist of co-ordinated contractions of the same frequency as the normal menstrual contractions of the uterus described by H. Hinselmann[7] and by H. Schröder,[8] and it is suggested that these are responsible for the expulsion of menstrual fluid.

Additional evidence suggesting a physiological role of these substances comes from the fact that they can be detected in premenstrual but not in pre-ovulatory endometrium, and have been found in the circulating blood during menstruation but not eight days later. Pickles puts forward the view that the normal contractions of the menstruating uterus may be explained as the myometrial responses to a substance with the properties of the menstrual stimulant which passes from the endometrium to the myometrium, either by some local route or through the general circulation. It is obviously possible that this mechanism could also be the basis for the abnormal contractions which occur in dysmenorrhoea. In this respect it is perhaps striking that the most sensitive human myometrial strips used by Pickles came from a 44-year-old patient's uterus which had been removed for incapacitating dysmenorrhoea.

[1] Smith, O. W., *Amer. J. Obstet. Gynec.*, 1947, **54**, 201.
[2] Smith, G. V. S., ibid., 1947, **54**, 212.
[3] Pickles, V. R., *Nature (Lond.)*, 1957, **180**, 1198.
[4] —— *J. Endocr.*, 1959, **18**, Proc. i.
[5] Chambers, P. L., and Pickles, V. R., *J. Physiol. (Lond.)*, 1958, **144**, 68.
[6] Pickles, V. R., *J. Endocr.*, 1959, **19**, 150.
[7] Hinselmann, H., *Zbl. Gynäk.*, 1925, **49**, 2386.
[8] Schröder, H., *Z. Geburtsh. Gynäk.*, 1927, **91**, 683.

Drug Treatment of Disease

SEDATIVES FOR CHILDREN

BY

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Vast sums of money are spent on the new tranquillizing drugs, but the evidence that the great majority of them achieve anything more than the simple, inexpensive, time-honoured drugs chloral, phenobarbitone, and aspirin is either extremely tenuous or non-existent. In any case it must always be remembered that these drugs do not cure the underlying disease, for they can only relieve symptoms. In all cases mentioned below the first essential is to treat the causative disease or emotional problem. It is interesting to note that at the Children's Hospital, Sheffield, with approximately 6,000 admissions and 8,500 new out-patients a year, the total spent in 1959 on the new tranquillizing drugs was £8, most of which was spent on meprobamate for the treatment of epilepsy (without much success), rather than for its purely sedative action. It may be argued, of course, that we should have used these drugs a great deal more.

There is very little occasion for using sedative drugs for long periods. In general they should be used in adequate dosage for short periods, and not for chronic cases. It should also be remembered that the child's symptoms can sometimes be relieved more successfully by giving a sedative drug to the mother rather than to the child.

Below I have listed the commoner conditions in children for which sedative drugs can often be profitably prescribed.

Cerebral Irritability in the Newborn Baby

Chloral in a dose of ½ to 1 gr. (30–60 mg.) may be given by mouth at intervals of two to four hours. An alternative is a subcutaneous injection of sodium phenobarbitone ⅛ gr. (8 mg.).

Evening Colic in the First Three Months

Having satisfied oneself that the diagnosis is correct, that the baby is not howling because he is hungry and that he is not crying merely because he wants to be picked up and played with (i.e., he continues to cry even when picked up), one should give dicyclomine hydrochloride syrup ("merbentyl"), in a dose of ½ to 1 teaspoonful (5–10 mg.) 20 minutes before the evening feed which has been found to precede the pain.

It should not be forgotten that infants grow out of the colic by the age of 2 to 3 months, so the medicine should by then have been discontinued. The cost is about 1d. per dose. Suffering parents would think that that was cheap even if they had to pay for it out of their own pockets.

Sleeplessness in Infants and Toddlers

The first essential is to deal with the management of the bad habits which have been allowed to develop. These consist chiefly of picking the baby up from his cot as soon as he whimpers, taking him downstairs as soon as he cries, sitting and playing with the child because he will not otherwise go to sleep, repeatedly going in to see the child to see if he is still breathing (so that he gets to expect a visit from his mother and stays awake till she comes), taking the child into the parents' bed when he cries, and allowing him to sleep in the parents' room after night feeds have been dropped (usually between 2 and 3 months of age). When one of these bad habits has been allowed to continue for long, it is very difficult to break it, and the first few days of proper management can be helped by the use of a sedative drug. I know of nothing better than chloral for the purpose. I tell mothers to begin with 5 gr. (350 mg.), and if that does not work to give 7½ gr. (0.5 g.) on the next evening, and if necessary 10 gr. (0.7 g.) on the next evening. The medicine is given about 20 minutes before the child goes to bed. Chloral is a safe drug. The hypnotic action is thought to be due to reduction to trichlorethyl alcohol, which is a cerebral depressant.

The taste is unpleasant, but it does not usually present much difficulty in a baby. The disadvantage of the chloral elixir for infants in the *B.N.F.* is the fact that 60 minims contain only 1 gr. of chloral.

It is quite useless to combine the chloral with potassium bromide, for there is no synergistic action between the two, and bromides have no effect until a certain serum-bromide level is reached after very large doses, or several days' administration.

Surprisingly enough the *B.N.F.* still contains a prescription for chloral with potassium bromide, after mentioning the fact that the sedative action of the mixture is entirely due to the chloral.

The chloral should be given for a few days only. There is no excuse at all for giving hypnotic drugs to children night after night.

Phenobarbitone for the purpose is useless. There is no evidence that the more recently introduced drug thalidomide ("distaval") possesses any advantage over chloral apart from its better taste, and it costs about 40 times more. It may be useful for infants who refuse to take chloral.

Teething

Much of the crying which is commonly ascribed to teething is due not to teething but to the formation of bad habits in connexion with sleep, as mentioned above.

If the baby really has discomfort from teething, aspirin is the drug of choice, in a dose of 2½ to 5 gr. (0.15 to 0.3 g.) at night not repeated until the next night.

Convulsions

Space will not permit a discussion of the treatment of epilepsy.* When a child is seen in a convulsion, the best immediate treatment, if it does not terminate spontaneously, is an intramuscular injection of

*This was the subject of an article in this series by Dr. Denis Williams, *Brit. med. J.*, 1958, **2**, 1155.

paraldehyde into the middle of the outer aspect of the thigh, in the following dosage:

Under 3 months	½ ml.
3–6 months	1 ml.
6–12 months	1.5 ml.
1–2 years	2 ml.
2–5 years	3–4 ml.

An alternative treatment is sodium phenobarbitone by intramuscular injection in the following dosage:

3 months	¼ gr. (16 mg.)
3 to 12 months ..	½ gr. (32 mg.)
2 years	½–1 gr. (32–65 mg.)

It is vital that the cause must always be sought, and in all cases hospital investigation should be carried out. In the case of suspected febrile convulsions a lumbar puncture should always be performed to exclude meningitis.

A convulsion due to acute nephritis necessitates immediate hospital treatment. The child is likely to be given 1–2 oz. (28–57 ml.) of 50% magnesium sulphate per rectum, or (preferably) a ganglion-blocking agent.

A convulsion due to tetany likewise calls for hospital treatment, because the cause must be determined. The child is likely to be given 3 to 10 ml. of 10% calcium gluconate intravenously.

Nervousness, Nervous Habit, Tics, School Phobia

I am constantly impressed by the number of children who have been given sedatives for these conditions, and especially for tics. In my opinion there is only rarely a place for barbiturates or other sedatives here. Tics, in particular, are totally unaffected by them. I have tried tranquillizing drugs as an adjuvant in the treatment of school phobia without any success.

Most of the drugs used have a potentially harmful effect. It is not sufficiently realized that phenobarbitone may have the opposite of the effect desired, aggravating chronic anxiety and worsening irritability and bad behaviour. There is probably no place for bromides here; they are cumulative in action, and may cause annoying rashes, depression, and other untoward symptoms. Tranquillizing drugs are of very doubtful and certainly unproved value in these conditions, and may have serious toxic actions.

The treatment of all these conditions depends not on medicine but on a thorough review of the child's environment and management. In the first place, much of children's nervousness of which parents complain is entirely normal for the age, and calls for no treatment at all. In other cases, in which nervousness is excessive, the child takes after his parents in that respect, and medicine will not alter it. As for tics, the essential thing is for the parents to ignore them. If they are getting on top of the parents, the parents may themselves be given a sedative, but not the child. School phobia is best dealt with by thoroughly investigating the home and school environment, remembering that in the great majority of cases the trouble lies in the parental attitudes, rather than in the school.

Hyperkinesis

In the great majority of cases mothers' complaints of overactivity of their child are allayed by reassurance that he is entirely normal, and that normal small children (especially around the 6-year-old period) do not sit still. In my opinion it should be most exceptional to give any medical treatment for a hyperkinetic child of normal intelligence. If the hyperkinesis is seriously interfering with school work, which must be very exceptional, I would try, for a short period only, one of these drugs: dexamphetamine, meprobamate, or chlorpromazine. There have been many reports about the effectiveness of dexamphetamine for the purpose, though one would have expected it to have the opposite effect. I have tried it on a few children myself, without success.

The aimless overactivity of mentally defective children is very distressing to parents. Many have found that dexamphetamine in a dose of 10 to 20 mg. per day is useful for the purpose, but I have not been impressed by it in cases which I have treated myself. Tranquillizing drugs may well be tried, and in severe cases even prolonged administration may be justified. I have tried meprobamate in doses of 200 to 800 mg. four times a day at the age of 5 to 12 years, but found it of value in one or two only. The toxic actions include insomnia, vomiting, urticaria, anaphylactoid reactions, bronchospasm, oedema, and arthralgia, with tremors and anxiety on withdrawal. In solution it is very unpleasant to take. Chlorpromazine in a dose of 1 mg. per kg. per day (usually 30–150 mg. per day at the age of 5 to 12 years) may be worth trying. Untoward symptoms include tremors, hepatitis, rash, oculogyric crises and other Parkinsonian symptoms, agranulocytosis, nasal congestion, and unexplained fever.

Acute Psychotic Anxiety

If phenobarbitone fails, I would try meprobamate or chlorpromazine.

Chorea

In conjunction with such specific treatment as may be indicated (such as steroids with salicylates if there is an active rheumatic process with carditis) one would give phenobarbitone by mouth in a dose of ½ gr. (32 mg. twice a day) at the age of 5 years.

Premedication

There is a difference of opinion on whether premedication before anaesthesia is desirable for children or not. Some feel that proper explanation of what is going to happen, with kind and wise management by all concerned with the child, is of greater value than any medicine. Others advocate that all children, or at least those liable to show anxiety about operative procedures, perhaps because of a previous unfortunate experience, should be given a sedative prior to anaesthesia.

For a baby prior to operation for pyloric stenosis under local anaesthesia, chloral by mouth in a dose of 1 gr. per lb. (140 mg. per kg.) (usually 6 to 10 gr. or 400 to 650 mg.) is satisfactory. For older children quinalbarbitone ("seconal") may be given in the following dosage:

1–2 years	½ to 1½ gr. (32 to 97 mg.)
2–6 years	1½ to 3 gr. (97 to 190 mg.)
6–12 years	3 to 7 gr. (190 to 450 mg.)

The maximum safe dosage is 0.1 gr. (6.5 mg.) per lb. (13 mg. per kg.). A dose of ¼ gr. costs approximately a farthing.

The old combination of morphine and atropine remains a satisfactory mixture for premedication. It seems that methylpentynol is not of value for premedication, and it is unpleasant to take.

Sedation Before Minor Surgical and Other Procedures

For minor procedures, such as the careful examination of an optic disk, or an encephalogram, rectal thiopentone is recommended. An enema is given if there is constipation. No food is given for at least three hours before the thiopentone. A hypodermic injection of atropine 1/150 or 1/100 gr. (0.43 or 0.65 mg.) is given half an hour before the thiopentone. The thiopentone is dissolved in 20 to 40 ml. of warm tap-water and injected slowly into the rectum by a rubber catheter. The buttocks are then held together to prevent the drug being returned. The dosage is as follows:

Dosage Schedule of Thiopentone for Children Weighing up to 52½ lb. (23.8 kg.)

Weight of Child lb.	kg.	Dose of Thiopentone
7.5–12.5	(3.4– 5.7)	0.2 g.
12.6–17.5	(5.7– 7.9)	0.3 g.
17.6–22.5	(8.0–10.2)	0.4 g.
22.6–27.5	(10.3–12.5)	0.5 g.
27.6–32.5	(12.5–14.7)	0.6 g.
32.6–37.5	(14.8–17.0)	0.7 g.
37.6–42.5	(17.1–19.3)	0.8 g.
42.6–47.5	(19.3–21.6)	0.9 g.
47.6–52.5	(21.6–23.8)	1.0 g.

Post-operative Treatment

For the relief of pain, tinct. opii B.P. in a dose of 1 minim (0.06 ml.) per year of age (sometimes with 2 additional minims for older children) is very effective.

Pethidine in a dose of 50 to 75 mg. by mouth is effective, but perhaps not quite so effective as tinct. opii B.P. It is slightly more expensive if given by mouth, but about 10 times more expensive than nepenthe if given by injection.

Cough

In my opinion there is very little need to give sedative cough medicines to children. Most coughs in children are productive, so that cough suppressants, such as codeine or pholcodine, are definitely contraindicated. A cough on going to bed is commonly due to a postnasal discharge, and neither suppressants nor expectorants are helpful. There is probably nothing better than the simple linctus for infants B.P.C., or opiate linctus of squill for infants—each in a dose of 60 minims (3.5 ml.). For a dry, irritating, unproductive cough, the codeine mixture for infants B.P.C. is adequate.

The first essential in the treatment of cough in children is to treat the cause. This may involve giving the appropriate antibiotic or bronchodilator drug, the treatment of an antrum infection, or the removal of adenoids.

Migraine

For the treatment of an attack of migraine, the most useful drugs are aspirin, tab. codein. co., "cafergot," and "migril." The difficulty with all these drugs is the fact that they may not be retained on account of vomiting. Aspirin and tab. codein. co. are each effective in most cases. Cafergot contains 100 mg. of caffeine and 1 mg. of ergotamine tartrate, and migril contains ergotamine tartrate 2 mg., caffeine (alkaloid) 100 mg., and cyclizine hydrochloride 50 mg. in each tablet. One tablet of cafergot may be given at the age of 5 years.

Frequent administration of the ergotamine drugs should be avoided because of the theoretical risk of ergot poisoning.

Migril is twice as expensive as cafergot and more than 50 times as expensive as aspirin, so that aspirin, being very effective and the cheapest, should be used first. Tab. codein. co. might be tried second if aspirin does not prove satisfactory.

Itching

As an adjuvant for the treatment of eczema, phenobarbitone or an antihistamine drug such as mepyramine maleate ("anthisan") may be used. A dose of 30 minims (1.8 ml.) of the elixir containing 12.5 mg. may be given to an infant under 1 year. At the age of 2 to 3 years the equivalent of 25 to 50 mg. may be given. The taste is unpleasant. Promethazine hydrochloride may also be used, though it is more expensive than mepyramine. At the age of 2 to 5 years 5 to 15 mg. may be given as a dose.

CELL PHYSIOLOGY IN CANCER

[FROM A SPECIAL CORRESPONDENT]

The 14th annual symposium on fundamental cancer research was held at Houston (Texas) on February 25–27 under the title of "Cell Physiology and Neoplasia." There were about 450 participants, mostly from the United States.

Several papers dealt with the properties of malignant cells. Dr. A. B. NOVIKOFF (New York) described how far staining methods for detecting enzyme activity have progressed in the past few years, particularly on the intracellular level. Biochemical, cytochemical, and electron-microscope studies now combined to give information of the highest value. He described differences between normal liver and three rat hepatomas revealed by the combined approach he was advocating, and he had high hopes that by studying tumours with graded malignancy and growth rate in such a manner we should come nearer to detailing the cell's transformation to malignancy as distinct from a phase of rapid division. Dr. S. KIT (Houston) compared various fractions of nucleic acids from normal and malignant tissues. He presented extensive data on spontaneous primary and transplanted lymphomas and normal spleen, stressing the technical requirements necessary to reveal differences in base sequence along polynucleotide claims. Dr. W. S. BECK (Boston) discussed the biochemistry of ribonucleic acid (R.N.A.), and its precursors in relation to malignancy. He commented on the significance of differences between the R.N.A. metabolism of normal and neoplastic cells, of which advantage could be taken in chemotherapy. Dr. C. LEUCHTENBERGER (Boston) demonstrated by spectrophotometric methods variation of deoxyribonucleic acid (D.N.A.) in tumours, both human and experimental. In normal tissues the D.N.A. pattern was constant and orderly, in benign lesions and malignant tissue the D.N.A. content of cells was increased and showed a much larger variation from cell to cell.

Chromosome Studies

Professor P. C. KOLLER (London, England) reviewed chromosome studies of tumours. He illustrated that in cells of experimental tumours deviation from normal was frequent, though such abnormalities were probably secondary phenomena. He had found no evidence to show that grossly visible chromosome changes were the

prime cause of malignancy. Dr. D. YERGANIAN (Boston) presented his studies on carcinogenesis in the Chinese hamster which, having a low number of chromosomes, provides suitable material to correlate chromosome behaviour with neoplasia. He found no association between malignant transformation and chromosomal abnormality.

The infection of Ehrlich ascites carcinoma cells with meningoencephalomyelitis R.N.A. was discussed by Dr. J. COLTER (Philadelphia), and he described the conditions required for effective infection. Dr. J. P. CHANG (Houston) had followed by cytochemical methods the enzymatic changes developing in rat's liver during the first two weeks after feeding with 3-methyl-4-dimethylaminoazobenzene. His techniques revealed changes long before morphological changes were apparent. Dr. L. DMOCHOWSKI (Houston) reported on electron-microscope studies of avian and mammalian (including human) tumours, and Dr. W. R. DURYEE (Washington) considered the host-virus relationship in the adenocarcinoma of the frog's kidney. Nuclear transplantation as a technique in studying neoplastic processes was described by Dr. T. J. KING (Philadelphia).

The Bertner Foundation award was presented to Dr. E. V. COWDRY (St. Louis) who also delivered the Bertner lecture on "The Lives of Cancer Cells."

HOSPITAL BUILDING IN NORTHERN IRELAND

Speaking in Belfast last week, the Minister of Health and Local Government for Northern Ireland, Mr. J. L. O. ANDREWS, expressed his gratitude for the help and co-operation given to his department by the Ministry of Health in London. Judging by the progress being made with hospital building in Northern Ireland it is Mr. Walker-Smith who ought to be thanking his opposite number in Stormont for welcome opportunities to learn from the pioneering experience of a keen and progressive hospital authority.

The Northern Ireland Hospitals Authority serves a population of 1,500,000—about the same as the East Anglian Regional Hospital Board—and the capital expenditure on hospitals per head of population in 1958–9 was 35s. 9d. The equivalent figure in England was 9s. 2d., in Scotland 11s. 10d., and in Wales 13s. 1d. This great difference is explained by the inadequacy of many of the hospitals in Northern Ireland—particularly the old Poor Law hospitals—when the National Health Service came into being in 1948. Patching, renovating, and adapting—processes all too familiar to hospital administrators in England—were not enough: new hospitals had to be built if the people in Northern Ireland were to have a health service comparable with that provided elsewhere in the United Kingdom. As a consequence, about £15m. has been spent to date on the provision of new buildings, and over the next ten years or so another £20m. will probably be spent.

Altnagelvin Hospital

The Northern Ireland Hospitals Authority, the chairman of which is Mr. W. MCKINNEY, has already collected a gratifying bunch of "firsts" in the hospital field. Most impressive in size and boldness of design is Altnagelvin Hospital, just outside Londonderry—the largest new complete general hospital built since the war in Britain. The estimated cost of the completed building is £2,500,000.

Opened in February, the hospital now has 300 patients, will soon have 400, and eventually may be enlarged to take 600. The main building is L-shaped and has 11 floors above ground level. From nearly all the wards, but particularly from the children's ward at the top, the countryside can be seen for miles around. There are no large wards, the standard unit for a ward sister being one six-bedded ward, five four-bedded wards, five single-bedded wards, and a day-room. Well away from the huge main building are the separate service departments—kitchen (connected by a long underground passage to the hospital), boiler-house, and laundry. The 50-acre site also holds the nurses' home and recreation hall, the matron's bungalow, and houses and flats for the resident medical staff (there is no medical superintendent).

By tradition many of the farming families in Northern Ireland send one or two daughters in each generation to train as nurses, and consequently hospitals with strong local attachments, as most of them have, are not usually very short of nurses.

Mental Hospitals

Only a few miles from Altnagelvin Hospital is the Gransha Hospital, Londonderry, the first mental hospital to be built in the United Kingdom since the war. The estimated cost of this hospital is £2m. Built on the villa system, about 800 beds are to be provided, but so far the new buildings comprise an admission block for 60 patients, villas for 90 patients, a convalescent unit for 28 patients, staff accommodation, and an administrative block. The work of the hospital is based on the system developed at the Mapperley Hospital, Nottingham.

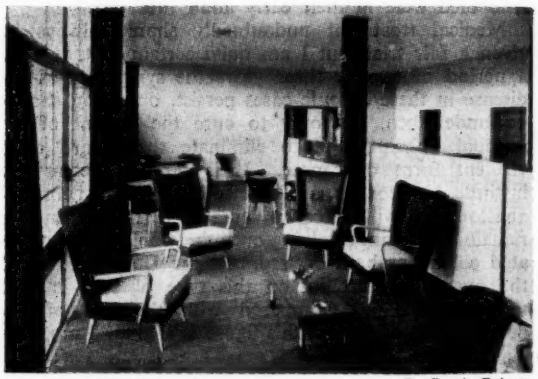
Between Londonderry and Belfast, at Muckamore Abbey in Co. Antrim, is the first colony for "persons requiring special care" (known elsewhere as "mental defectives") ever to be built in Northern Ireland. This institution is also estimated to cost £2m. It will hold just over 1,000 patients in 23 villas, but so far buildings for only half this number have been completed. A notable feature of the colony will be a school to accommodate 350 children not considered educable by ordinary standards.

Altnagelvin Hospital.

There are probably about 8,000 to 10,000 persons requiring special care in Northern Ireland, of whom about 3,500 are in the care of the hospital service. (In Northern Ireland the hospital authority is responsible for the care of these patients, whether they are at home or in hospital.)

Hospitals in Belfast

Best known of all the hospitals in Northern Ireland is the Royal Victoria Hospital, Belfast. This, with its associated hospitals, forms the only teaching group in the country. With over 1,300 beds, 36,000 admissions per year, and 500,000 out-patient attendances, the group performs an invaluable service to the community, providing some specialist services unobtainable elsewhere. Many of the buildings are out of date, but they cannot be replaced before other more urgent work is finished. Meanwhile planning for the future continues, and much reorganization has already been completed. One of the newest buildings on the site is the Institute of Clinical Science built by Queen's University as part of its medical faculty and opened in 1954.



[De Burgh, Galway

Day room in Nuffield House.

The Musgrave Park Hospital in Belfast has provided the site for one of the most important experiments in hospital design ever undertaken in the United Kingdom. Here the Nuffield Provincial Hospitals Trust co-operated with the Northern Ireland Hospitals Authority to build a two-story, 80-bedded surgical unit. Coming into use eighteen months ago, this unit is known as Nuffield House: it incorporates the latest ideas in design with the use of the most modern equipment for all purposes from disposal of waste to the cleaning of instruments and the storage of dangerous drugs. The sister of each of the two wards has 40 patients in her charge divided into two groups of twenty. Each group is in the care of a team of five nurses. Of these 20 patients four are in single rooms, and the remaining 16 are divided among two ward units of six beds each and one of four. A notable feature of the ward is the large and pleasant day-room, which is designed to give the patients a feeling of privacy while allowing the nurses to keep an eye on them.

Last but not least of Belfast's new hospital projects is Wakehurst House, the first hospital in the British Isles to be built for the active treatment of the elderly. It forms part of the Belfast City Hospital, and the new building, with 80 beds and physiotherapy and occupational therapy departments, cost £200,000. Each of the two wards of 40 beds is divided into two separate sections, one for patients being actively rehabilitated and one for long-stay patients. As at Nuffield House, the day-space is notable. In addition to a sitting-room there is plenty of room near their beds for the patients to practise walking and other exercises. About 800 patients were returned to their homes last year from this geriatric unit, an impressive figure which shows what can be done for the elderly patient crippled by illness or injury (the average age in Wakehurst House is about 75) if the right facilities are provided.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Pathology for the G.P.

SIR,—Dr. S. L. Henderson Smith (*Journal*, March 5, p. 725) has raised the problem of providing a necropsy service for G.P.s.

In the Annual Report of Council for 1957 (*Supplement*, April 13, 1957, p. 169) it was stated that the principle of providing such a service and paying for transport from public funds had been accepted by the Ministry of Health. I had assumed from this that the barrier of cost had thus been removed, and in this Group we have, on several occasions, carried out investigations of this sort with the full co-operation of the finance officer. He tells me, however, that he has never seen any regulation which specifically authorizes payment of this sort and has been acting on his own initiative. Evidently not all finance officers are so enlightened.

If it is the case that no such regulation exists, then it is surely desirable that the Ministry should authorize officially a practice which they have apparently agreed in principle.—I am, etc.,

Department of Pathology,
Bedford General Hospital. J. C. VALENTINE.

SIR,—Dr. S. L. Henderson Smith (*Journal*, March 5, p. 725) has drawn attention to a common deficiency in the pathological services available to the G.P.—namely, the post-mortem examination. A good many deaths in general practice are properly dealt with by the coroner, either because the G.P. has not seen the patient within 14 days of death, or because the cause of death is so obscure that the G.P. cannot honestly complete a certificate which will satisfy the registrar ; in such natural deaths the coroner can order a post-mortem examination without inquest, and in this area he usually does so in cremation cases to save the relatives the embarrassment of a last-minute necropsy at the request of the medical referee. There remain those cases in which a necropsy is desirable, subject to the consent of the relatives, in the interests of medical research. These ought to be covered by the hospital pathological service, but the chief obstacle is the cost of transporting the body.

In this area the problem has been solved quite simply. The G.P. discusses the case with me on the telephone, and, if I am satisfied that the death is outside the coroner's jurisdiction and that a necropsy is nevertheless desirable, I arrange with a local undertaker to bring the body to the hospital mortuary and to return it afterwards. The undertaker employed for this purpose has a contract with the hospital management committee, who pay his charges at an agreed rate. There is, of course, no charge for the examination. So far as I know there is nothing in the regulations to prevent any hospital management committee from adopting such a course if the pathologist asks for it. In eight years' experience of this service I have found that it is seldom used, but on those rare occasions it is invaluable.—I am, etc.,

Pathology Laboratory,
Barnstaple. R. B. H. TIERNEY.

SIR,—I regret that in my article on this subject (*Journal*, February 6, p. 415) I did not mention post-mortem examinations for the G.P. Of course we provide this service, and it is asked for with moderate frequency. We have indeed carried out a partial confirmatory post mortem in the home of the deceased, but normally the body is brought to the hospital mortuary. This is shortly to be enlarged and become a joint mortuary of the hospital and the Borough of Kingston-upon-Thames, so that all this type of work, whether from the hospital or the coroner, will be done under the one roof.

With regard to G.P. cases, we have to lay down certain conditions. The usual procedure is for the G.P. to ring the morbid anatomist and give a few details. He is then asked (1) to get consent, preferably written, from the next of kin, (2) to assure the pathologist that there is no question of reporting to the coroner, (3) to ring the undertaker and have the body sent to the hospital mortuary, (4) to set a time when he can watch the P.M. We have, so far, had no difficulty over transport. The ambulance cannot, of course, be used for the transport of dead persons, but the undertakers in this area are always very willing to co-operate, and, since many bodies are in any case moved to undertakers' chapels, there is usually very little difficulty in getting the additional service of bringing a body to our mortuary and removing it again later, since they are here all too frequently. I think Dr. S. L. Henderson Smith (*Journal*, March 5, p. 725) will find that this service is available in other areas, and, provided the laboratory is prepared to do such examinations, there is nothing in the N.H.S. regulations to prevent them doing so.

Perhaps I should add that we have a number of small hospitals without post-mortem rooms, and the bodies are brought from them to the central mortuary. In this case the hospital management committee can pay for transport.—I am, etc.,

Kingston-upon-Thames. D. STARK MURRAY.

SIR,—Dr. S. L. Henderson Smith (*Journal*, March 5, p. 725) may be cheered to know that there is no reason why he should not have the services which he requires and at present lacks. The hospital management committtee is permitted to pay the cost of transport of the body to and from the hospital. It is necessary to get the support of the pathologist, who gets no extra remuneration for these P.M.s. We have this facility in this area, the H.M.C. having agreed to pay the transport cost, after being approached by the local medical committee. Discretion is given to the pathologist to refuse in a particular instance.

Credit for the granting of this permission to H.M.C.s must go to the B.M.A. negotiators.—I am, etc.,

Risca, Mon. MICHAEL WADE.

*** The following statement appeared in Annual Report of Council for 1957 (*Brit. med. J. Suppl.*, 1957, **1**, 169): "The G.M.S. Committee . . . secured the Ministry's agreement to the suggestion that, when a general practitioner requires a necropsy, if the pathologist agrees, then the cost of transport from home to hospital should be met from public funds."—ED., *B.M.J.*

SIR,—If it had occurred to him Dr. S. L. Henderson Smith (*Journal*, March 5, p. 725) could have made his own post-mortem examination by making use of the coffin-lid upside down as a slab. The late Mr. T. S. P. Strangeways suggested this to me, and I have found it very convenient in the few which I have made or helped to make. The question of payment did not arise, because the examinations were made only to satisfy our own scientific curiosity.—I am, etc.,

Beckenham, Kent. W. M. PENNY.

Conservative Treatment of Ulcerative Colitis

SIR,—I share Dr. R. W. Cockshut's concern (*Journal*, March 5, p. 731) with regard to the development of cancer in the long-standing case of ulcerative colitis. It is a complication to which those who have developed the disease in their youth seem particularly prone and one which is so insidious in its onset that its diagnosis in most cases is virtually impossible until widespread and incurable metastases have taken place. Amongst 140 cases under my care between March, 1952, and August, 1959, there were 10 patients in whom the complication had arisen, an incidence of 7%. Of these only one remains alive, and with two exceptions all who died were in their early adult life.

Medical treatment undoubtedly should always be given a fair trial, but I am quite certain that, if after a period of two or three years the symptoms of the disease in these chronic cases persist, operation should be undertaken, not only to cure the patient of his residual ill-health but to eliminate the hazard of a virulent form of cancer. It is rarely necessary to institute an ileostomy. Total colectomy and ileorectal anastomosis will effect a cure, the disease in the remaining rectum resolving once the whole of the ulcerated colon has been excised. At the Gordon Hospital the operative mortality on this type of case is little more than 1%. Compared with the risk of the development of cancer, this figure is slight.—I am, etc.,

London, W.1. STANLEY AYLETT.

Dangers of Halothane

SIR,—It is now well known that patients being anaesthetized with halothane in the closed-circuit apparatus may suddenly develop cardiovascular and respiratory depression, and must therefore be watched with the greatest of care. The use of low concentrations of halothane from a calibrated vaporizer on a semiclosed circuit has been considered to be relatively trouble-free. The three incidents described below indicate that this is not so, and that equal vigilance is required when halothane is given in a semiclosed circuit.

Case 1.—A male of 40 years was to undergo right frontal craniotomy for a large craniopharyngioma. He had a history of angina of effort and left ventricular strain. Occasional extrasystoles were apparent before operation. Premedication was with atropine 0.6 mg. by subcutaneous injection. Anaesthesia was induced with thiopentone 500 mg. and succinylcholine chloride 40 mg., followed by tracheal spraying with 4 ml. lignocaine hydrochloride 4%. A No. 10 flexometallic tube lubricated with lignocaine ointment was passed and the lungs inflated with nitrous-oxide (6 litres per minute) and oxygen (2 litres per minute) with a semiclosed circuit. Spontaneous respiration returned rapidly and the pulse was normal. Halothane 0.5% was added and then increased to 1%. Suddenly, after three minutes on this mixture, while the E.C.G. leads were being applied, the pulse became grossly irregular and of very poor volume, and the respiration very shallow. The halothane was turned off and the lungs inflated with oxygen. The tidal volume and pulse volume rapidly improved, but the arrhythmia persisted on nitrous oxide and oxygen for three to four minutes until diethyl ether was added. The pulse

rhythm then became normal except for occasional extrasystoles. The patient was transferred to the theatre, the ether discontinued, and a trace of trichlorethylene substituted. During the three-and-a-half-hour operation the E.C.G. remained normal and maintenance was satisfactory with trichlorethylene. The patient made an uneventful recovery.

Case 2.—A fit male patient of 27 years was undergoing excision of a protruded intervertebral disk. He was premedicated with "omnopon" 20 mg. and scopolamine 0.4 mg. Anaesthesia was induced with thiopentone 600 mg. and succinylcholine chloride 40 mg., followed by lignocaine spraying of the trachea and intubation with a No. 10 flexometallic tube. Anaesthesia was maintained with nitrous-oxide (6 litres per minute) and oxygen (two litres per minute), with 0.5% halothane from a "fluotec" using a semiclosed circuit. Anaesthesia was satisfactory, the blood pressure being 90/60 mm. Hg and the pulse rate 70 per minute. Suddenly in the course of the operation the blood pressure dropped to 44/30 mm. Hg and the pulse rate to 44 per minute. The halothane was turned off and atropine 0.3 mg. given intravenously, with immediate recovery. The operation was completed on nitrous oxide and oxygen alone, and the patient made a satisfactory recovery.

Case 3.—A fit man aged 62 was scheduled for haemorrhoidectomy. Premedication was by pethidine 100 mg. and atropine 0.8 mg. An uneventful induction of anaesthesia with thiopentone 500 mg. was followed by nitrous-oxide and oxygen with 1% halothane in a semiclosed circuit. Anaesthesia remained quite smooth until the operation was almost finished, when respiration suddenly ceased, the pulse, which had been steady at 70 per minute, became imperceptible, the pupil dilated widely, and the colour became ashy grey. Immediate emptying of the reservoir bag and rhythmic inflation of the lungs with 100% oxygen were carried out, and in just over a minute the pulse suddenly returned, the face flushed, and the pupil contracted. Shortly afterwards a sighing respiration was noted (in both patient and anaesthetist) and the unnerving incident was over.

It will be evident from these three reports that cardiovascular collapse from low concentrations of halothane may occur suddenly at any stage of the operation even in fit patients. Its occurrence is not exclusive to closed-circuit techniques. Halothane is being widely used by anaesthetists at all stages of their careers, and, while its advantages are well recognized, its dangers must not be overlooked whatever technique is used.—We are, etc.,

C. LANGTON HEWER.
R. I. BALLANTINE.

Department of Anaesthesia,
St. Bartholomew's Hospital,
London, E.C.1.

Brain-washing

SIR,—On February 28 it was reported in the *Observer* that a recent discourse to the Royal Institution had been on the subject of "Scientific Lessons of Brain-washing." The report reveals that during the war captured enemy agents were subjected to a series of events which had as their aim the production of a severe neurotic illness with delirium during which a confession was extracted from the victim.

Briefly the process appears to have been as follows: the prisoner was exposed to moderate physical discomfort, cut off from all contact with the outside world, and poorly fed at irregular intervals. In consequence he became disorientated and confused. The interrogator then questioned him, and, noting what subjects produced mental tension, deliberately linked these with a noise or gesture of his own. Eventually a conditioned reflex became established whereby the interrogator could produce great emotional stress in the prisoner at will. The process was continued relentlessly until the prisoner, in a state akin to severe neurosis, would make a "confession," which included betrayal of his previous beliefs and denunciation of former colleagues. It is noteworthy that at no time was the prisoner subjected to physical torture, not apparently for moral or legal reasons, but because it was known that this would produce a strengthening of resistance and immunity to further inquisition.

To me this so-called interrogation is odious in the extreme, but what is worse is that such a programme could not have been devised without the assistance of qualified medical practitioners who must have been well aware that their medical knowledge was being used for purposes opposed in every way to the ethical practice and beliefs of their profession.

Unfortunately, for security reasons, we shall never be allowed to know which of our colleagues have disgraced us in this inexcusable fashion, and can only condemn them *absente reo*. Nevertheless, I trust the Association will not hesitate to take steps to bring to the notice of the authorities concerned the overwhelming disgust felt by its members at this ignoble prostitution of medical knowledge and will make every endeavour to prevent medical practitioners again being induced to take part in such proceedings.—I am, etc.,

Hull, Yorkshire. RAY L. LUFFINGHAM.

*** This matter has been discussed in Parliament (see report on page 886).—ED., *B.M.J.*

A New Exanthem ?

SIR,—During the past five weeks or so I have seen a series of 15 cases of a condition which to my knowledge has not yet found its way into the medical literature.

The disease begins with upper respiratory catarrh which does not progress to actual rhinorrhoea. The patient is feverish but is not considered sufficiently unwell to require medical advice. These prodromal symptoms subside after a couple of days and are followed by the appearance of a characteristic rash. The eruption irregularly involves the face, trunk, and limbs. Constitutional symptoms do not accompany the rash, which remains for from five to seven days and then disappears without trace. Cervical adenitis is not a prominent feature of the condition at any stage.

The rash has two peculiarities which differentiate it from other exanthemata: its retiform morphology and its variability in emphasis. The eruption consists of an erythematous network in the skin made up of irregular gyrate and circinate areas, the enclosed skin appearing normal. The elements of this network vary in size up to an inch (2.5 cm.) in diameter. They occur in groups covering areas which measure several square inches in extent, mainly on the cheeks and neck, front of arms and forearms, front of thighs, and on the trunk. The eruption is not constant and may completely disappear from any area for several hours at a time. At other times, especially on the face and trunk, the flat macular network changes to raised, palpable, urticaria-like configurations, when the intervening normal skin may become involved. This change occurs in a few hours, the reverse process occupying a similar length of time. Several episodes of waxing and waning of individual areas occur during the course of the condition. No constitutional symptoms are complained of during the changes in the appearance of the eruption. It does not itch at any time. Desquamation does not occur.

The age-incidence is between 1 and 14 years. All contacts do not seem to be susceptible, but in three cases the incubation period was about three weeks. More males than females have been seen to date; this sex-distribution may be inherent in the small number of cases so far seen. Fresh cases are still being encountered. Throat-swabs of two patients in the catarrhal stage were negative for haemolytic

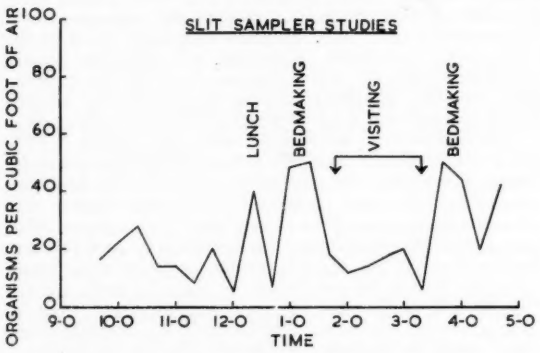
streptococci. Routine haematological investigation has not been attempted, since it could not be justified in such a mild self-limiting condition. The white cell total and differential count carried out on one patient on the third day of the rash showed no abnormality.

The aetiology of this condition is one for speculation. In the absence of haemolytic streptococci in the throats of two contacts and the lack of any complaint of preceding sore throats in all the cases so far studied, an atypical streptococcal erythrotoxin can probably be ruled out. It is suggested that the condition is due to a virus, and it may be that yet another orphan virus has found its parent disease. If this condition is in fact a new one, it should have a name. In view of its peculiar marble-like appearance in the macular stage, perhaps "marmorosis," while not being particularly euphonic, might be acceptable. "Erythema retiforme infectiva" would possibly appeal to the dermatologically inclined. "Reticella" (cf. varicella) or "reteola juvenilis—seventh disease" (cf. roseola infantum) might be preferred by the epidemiologists. Perhaps there is an official body which considers these matters and to which the problem—if the existence of the condition as a separate disease-entity is accepted—can be referred.—I am, etc.,

Plymouth. BERNARD PECK.

Hospital Infection and Visitors

SIR,—Professor A. M. Boyd paints a lurid picture of the possible dangers of infection spreading from patients' visitors to the patients themselves (*Journal*, February 20, p. 563). The potential danger of visiting hours concerned us also, and we have made one or two observations on this problem. As the accompanying chart shows, the bacterial contamination of the air of a surgical ward was low during visiting hours and very



much higher during such ward activities as serving of lunch and bedmaking. The visitors to the ward were questioned and we found none with coughs or colds (we carried out this investigation in November last year). We saw no boils or blains, and none of the visitors admitted to any skin infections.

We feel that Professor Boyd's comments may be couched in exaggerated terms. Are his wards really "invaded by hordes of visitors coughing, sneezing, some doubtless with boils and blains, and probably some with open tuberculosis"? Is this really followed by "an orgy of hugging, kissing, nose-scratching, pawing of patients and blankets"? Do they really leave the wards in a state comparable to "a down-town saloon"? Professor Boyd correctly points out that resistant strains of staphylococcus are responsible for the majority of surgical wound infections, excluding those infected from within at "dirty" operations. Surely he does not suggest that visitors are responsible for the introduction of *resistant* staphylococci to his wards? We feel that it is more likely that the hospital will infect the visitors than that the visitors will do much to infect the hospital.—We are, etc.,

L. STEINGOLD.
L. ASHWORTH.

Department of Pathology,
St. Andrew's Hospital,
London, E.3.

Paralysis in Morocco

SIR,—Your annotation (*Journal*, February 27, p. 630) contains the statement that the rabbit is very resistant to poisoning by *ortho*-cresyl phosphate. The rabbit is, in fact, highly susceptible to tri-*ortho*-cresyl phosphate, and for this reason was used routinely by Smith, Engel, and Stohlman[1] in their screening tests. Smith, Elvove, and Frazier[2] describe the response of the rabbit as characterized by tremors and spastic incoordination of the muscles of the extremities with later a generalized flaccid paralysis and death from respiratory paralysis.

Poisoning by tri-*o*-cresyl phosphate in the rabbit is atypical in three respects; first, the signs start earlier than in the chicken; second, the clinical effects differ in the two animals; and, third, the mortality is high in the rabbit. Barnes[3] has reproduced these signs, and states that the characteristic sign of intoxication in the rabbit is head-drop. Because of the atypical response in rabbits the mature chicken is the experimental animal normally used. Barnes and Denz[4] first showed the immunity of chicks to these classes of compounds by dosing them with di-isopropyl fluorophosphate. Cavanagh[5] has confirmed this finding with tri-*o*-cresyl phosphate, and recently Bondy, Field, Worden, and Hughes[6] have titrated single oral doses of 1,000 mg. tri-*o*-cresyl phosphate/kg. body-weight against age in young chicks and found no effect up to 50 days of age, but a marked neurotoxic effect at 72 days. Barnes[3] found that paralysis does not occur suddenly at a specific age—the effect is gradual after 50 days of age; for example, 60-day-old chicks suffer the paralysis, but, unlike their elders, recover rapidly.—I am, etc.,

Birmingham, 16. J. P. W. HUGHES.

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Therapeutic Abortion

SIR,—May I comment on Professor T. N. A. Jeffcoate's views (*Journal*, February 27, p. 581) on therapeutic abortion on psychiatric grounds? The experience of a consultant in this field is inevitably coloured by the fact that cases are referred to him in the light of his known attitudes. My own general practice experience suggests that termination is indicated more often than Professor Jeffcoate suggests. Certainly the figure of 0.8 terminations per 1,000 pregnancies (for all indications) must underestimate the problem. This figure was based upon an antenatal clinic population, and women who reject their pregnancies do not attend these clinics.

In my own practice of some 2,400 I have traced records of ten women who have had terminations of pregnancy on psychiatric grounds, the psychiatrists and gynaecologists concerned being on the staff of London teaching hospitals in all these cases. One of these patients had earlier been considered for termination but refused, following which she had made a determined suicidal attempt by gas. Records of seven other women who were referred for an opinion but in whom termination was not recommended have been traced. Two accepted their pregnancies, two were terminated medically abroad, and three had illegal abortions. A large number of other women have presented with unwanted pregnancies; some came to accept the pregnancy, but many, despite detailed and even exaggerated warnings of the dangers to life, health, and fertility involved, have proceeded with illegal abortions. Haemorrhage or sepsis occurs in the majority of these cases. Only one of the patients terminated on psychiatric grounds had an adverse psychological reaction, lasting a few months. While a determination to take the risk of an illegal abortion does not in itself constitute a legal justification for therapeutic abortion, it does provide evidence that the psychological distress occasioned by an unwanted pregnancy can be profound.

Prediction in psychiatry is less exact than in clinical medicine, but I do not think that consultants who accept psychological indications for termination are guilty of abuse or of errors of judgment; concern for the mother's health must include a realistic assessment of the risks of suicide and of illegal abortion. This is a distressingly common problem; in my own practice, over the past eighteen months, the number of pregnancies terminated, legally or illegally, corresponds to an annual rate of 2 per 1,000 population, or about one-seventh of the national birth rate. May I conclude by suggesting that this emphasizes the responsibility of the profession for securing the extension and widespread advertisement of family planning facilities?—I am, etc.,

London, N.W.5. ANTHONY RYLE.

Internal Tampons

SIR,—Obviously Dr. W. R. E. Harrison (*Journal*, March 5, p. 729) is not a female who has suffered from menorrhagia. Only those who have experienced the misery of having to play games and do gymnastics hampered by the chafing of a soaking and malodorous sanitary towel can appreciate how very unpleasant it is. Internal tampons may not cure dysmenorrhoea, but at least they relieve one of the chafing and of the unpleasant smell, of which a fastidious girl is all too conscious. Males resent incontinence of urine as much as do females, but it never seems to occur to the disapproving male doctor that the woman who does not use tampons has to put up with an equally uncomfortable state for an average time equivalent of one-fifth of each year. Moreover, I very much doubt whether any man would tolerate such discomfort if any alternative offered.

With regard to drainage, it is still accepted surgical practice to use a pack to drain a deep, dark cavity (for example, the perineal wound of a total cystectomy or an abdomino-perineal resection of rectum)—which is precisely what the vagina is. Few surgeons would accept a loosely applied surface pad as an alternative.

I also find it difficult to see what psychological harm tampons can do to a normal girl. After all, most females sooner or later have to get used to foreign bodies being introduced into their vaginas—and vaginismus and its minor variants in dyspareunia are still distressingly common complaints. If Dr. Harrison wishes to imply that the girl who uses tampons does so in order to obtain a perverted pleasure he is betraying a curious ignorance of female physiology: stimulation of the vagina arouses no erotic response at all unless it is preceded by adequate stimulation of the clitoris. In any case, those whose tastes lie in that direction will find plenty of other inserts besides tampons.—I am, etc.,

Royal East Sussex Hospital, Hastings. PAULA H. GOSLING.

Mothers' Preference in Confinement

SIR,—Sir Dugald Baird (*Journal*, February 27, p. 642) has given some cogent reasons for questioning the validity of the generalizations made by Drs. I. Gordon and T. F. Elias-Jones (*Journal*, January 2, p. 52) from their investigation of the mothers' preferences in confinement. We had noticed that the Ilford data were likely to be biased, owing to the method of selection which was adopted, and had constructed a hypothetical detailed analysis of part of their published results to estimate the magnitude of the bias. Our conclusion was that the preference rate of 80% for home confinements which was found by Drs. Gordon and Elias-Jones may be quite illusory. Some parts of our calculations were based on rather arbitrary assumptions, but, on comparison with the Aberdeen figures, it seems that they erred in favour of the Ilford thesis. The fact that the interim results from a similar investigation in Blackpool by Drs. D. W. Wauchob and D. P. W. Roberts (*Journal*, January 30, p. 349) agree with those of Ilford suggests that similar sources of bias are operating in both.

Suppose that 50% (i.e., 776) of the 1,552 mothers in the Ilford investigation were multiparae, and that, of them, 85% (i.e., 660) had their first confinement in hospital. (In Aberdeen, the corresponding proportions would have been 64% and about 98.3% respectively, increasing the estimated 776 to 998, and the estimated 660 to 980, with the Ilford total of 1,552.) Of these multiparae who had their first confinement in hospital, perhaps some 200 (= 30% of 660 or 20% of 980) deliberately had their subsequent (or, at least, their latest) confinement at home because of a distaste for hospital confinements against which there was insufficient medical indication for a repeated hospital confinement. This group of 200 mothers may be largely co-extensive with the group of 247 (=91.8% of 269, from Tables I and III of the Ilford report) mothers who preferred home and had their latest child at home, and whose preferences were recorded because they changed their place of confinement. On the other hand, some mothers, estimated very roughly at 415 (=63% of 660 or 42% of 980) from the data of the Ilford report, had all their confinements in hospital up to the time of the survey, but their opinions were disregarded; and also disregarded were some 25 or so mothers who had all their confinements at home. Instead of including these approximately 440 mothers who had kept to one place of confinement, the Ilford report completes the group of 336 mothers studied intensively by including some 136 (=336–200) mothers whose preferences might be expected to be heterogeneous, and thus, to some extent, to cancel one another out on a percentage basis. Some heterogeneity was also introduced if the mothers were not perfectly clear whether their preferences were to refer to their latest confinement or to their first or to some other defined circumstances. And, as Sir Dugald Baird has mentioned, it is very difficult to get trustworthy reasons for preferences by the method used in Ilford.

The accompanying table illustrates in more detail how the numbers reported or implied by Drs. Gordon and Elias-Jones might have arisen. The percentages given in their

Table III agree with those which can be calculated from these estimates.

To summarize: the Ilford report almost entirely ignores the multiparae whose preferences were so strong that they did not change their place of confinement, and no information is given as to how numerous they were,

Place of Latest Confinement	Place of First Confinement	Preferences			
		Home	Hosp.	Undecided	Discounted
Home (414)	Home (66)	41	—	—	25
	Hosp. (235)	206	13	16	—
	Primip. (113)	—	—	—	113
Hosp. (1,138)	Home (50)	22	25	3	—
	Hosp. (425)	—	10	—	415
	Primip. (663)	—	—	—	663
Totals (1,552)		269	48	19	1,216

although there may have been as many as 440 (=776−336) or even 662 (=998−336) of them. It also dismisses the preferences of the primiparae as being of relatively little interest. It does not indicate whether the mothers were quite clear as to the confinement to which their preferences were intended to refer. On the other hand, the group of 336 mothers whose preferences were analysed may have been largely self-selected in favour of home confinements. These considerations, and the additional ones given by Sir Dugald Baird, should be borne in mind in generalizing from data obtained in this way.—We are, etc.,

M. C. K. TWEEDIE.
JOYCE K. TWEEDIE.

Liverpool, 19.

SIR,—Sir Dugald Baird (*Brit. med. J.*, Feb. 27, p. 642) suggests that the conflict of evidence and opinion, between Drs. I. Gordon and T. F. Elias-Jones (*Brit. med. J.*, Jan. 2, p. 52) on the one hand, and Drs. D. W. Wauchob and D. P. W. Roberts (*Brit. med. J.*, Jan. 30, p. 349) on the other, arises from the restriction of their surveys by the former to mothers who have experienced both home and hospital confinement.

During the last two months we have asked mothers in this practice attending for antenatal care (whether booked for home or hospital confinement) their preference in this matter. Out of a total of 51 patients, 41 (80%) expressed a preference for home confinement. Of the total, 18 were primigravidae, and of these 14 (77%) wished to have their babies at home. The commonest reason given for preferring domiciliary confinement was that the mother felt happier in her own home among familiar faces and surroundings. Of the 10 mothers who preferred hospital delivery, five did so solely because they could not get enough help at home, three felt hospital delivery was safer, one thought she would get more rest there, and the other said that from previous experience a "hospital baby" did not cry at night.

These figures are admittedly small, but do support the contention that in some areas at least the majority of mothers prefer home to hospital confinement, and, furthermore, that this preference is not restricted to mothers who have experienced both.—We are, etc.,

G. H. FOWLER.
A. M. SWEET.

Oxford.

SIR,—In the *Medical Officer* last October I published a survey of "mother's preference" for confinement in Ealing, 1958[1]: 889 women who had been confined in 1958 were interviewed. 748 were given the booking they requested, and 214 of these chose a home confinement. The largest number of requests for hospital confinement were from primiparae, but the preferences of the multiparae were nearly equal: 194 in favour of home, and 196 in favour of hospital. Six multiparae stated that they would have preferred a home confinement if adequate and inexpensive domestic help had been available.

It is interesting that among those who had had confinements both at home and in hospital, the Ealing figures should be very similar to those obtained by Dr. Gordon in Ilford.

	Home	Hospital	No Preference
Ilford	80%	14%	6%
Ealing	79%	18%	3%

Sir Dugald Baird (*Brit. med. J.*, Feb. 27, p. 642) suggests that the results of the survey by Drs. I. Gordon and T. F. Elias-Jones (*Brit. med. J.*, Jan. 2, p. 52) may have been affected by the method of questioning. My questionaries were completed in retrospect by health visitors, who do not preach any policy about the place of confinement. If we cannot ask the mothers direct questions, how else can we know their views? Their preferences may well be dictated by their domestic responsibilities and not by their personal desires, but is this not the type of motherhood we want to encourage?

Applicants for hospital beds in Ealing are being turned away, but there are still many women who are happy and content with home confinement.—I am, etc.,

MARGARET MCDONALD.

Area Health Office,
Ealing, London, W.5.

REFERENCE

[1] McDonald, M., *Med. Offr*, 1959, **102**, 225.

SIR,—May I, as a G.P. and mother of four children, add my experiences and views to your correspondence on hospital *versus* home confinement? My first child was born in a war-time hospital. After six days I discharged myself, exhausted from lack of sleep, with a badly cracked nipple, inadequate advice on breast-feeding, and a baby with very sore buttocks. All my other children were born at home. I had adequate rest, breast-feeding was established easily, and all members of the family were present to welcome and celebrate the new arrival.

Hospital confinements have come to be regarded as the natural thing, and women tend to look at home confinements with horror. On the few occasions that I have persuaded intelligent multiparae to have their babies at home they have always been grateful and delighted, and, I feel, their relationship with the infant, and that of the older children with the new baby, have been much less strained. Most women go to the maternity home automatically, particularly in industrial areas. One reason, I feel sure, is that the additional grant for home confinements does not adequately cover the wages of a relative who has to stay off work or the payments to a home-help. The home-help usually arrives after the older children have gone to school and leaves before they return. She therefore appears to be of very little use to the family—if you can get her at all.

One way to ease the strain on maternity hospitals would therefore be to increase the financial inducement to home confinements. I still remain a firm believer in the fact that a new baby is a family acquisition, and should be a member of the family from the moment of birth.—I am, etc.,

ELENA ZADIK.

Leigh, Lancs.

Congenital Dislocation of the Hip

SIR,—For various reasons it is important to contradict Mr. Denis Browne's mistaken statement (*Journal*, February 20, p. 564) that limitation of abduction in a little child is in itself a reliable indication of congenital dislocation of the hip. The "sign" is not only present in conditions other than dislocation, but, what is more important, it is often absent when there is true congenital dislocation. The early detection of congenital dislocation of the hip has long been recognized to be of paramount importance, but it presents very great difficulty.

Perhaps I ought to add that the views of Mr. E. W. Somerville and Mr. J. C. Scott (*Journal*, March 5, p. 724) are not accepted by observers of greater experience especially in Scandinavia, Northern Italy, and parts of North America, where the incidence of congenital dislocation of the hip is infinitely greater than in the Oxford area. In the space reasonable for a letter in your journal, elaboration of my statement is impracticable.—I am, etc.,

Liverpool, 1. BRYAN MCFARLAND.

SIR,—I am indebted to Mr. Denis Browne for having stimulated my enthusiasm for the early diagnosis of C.D.H., and for his generous remarks (*Journal*, February 20, p. 564).

I think a comparison and a contrast can be made with paralytic polio, since the Public Health Service now tries, by a series of inoculations, to prevent the vast majority of those inoculated from reaching the orthopaedists. With regard to C.D.H., surely it should be the business of the Public Health Service, which sees about 75% of all babies in England and Wales, to try to ensure by frequent examinations in the first year of life that every case reaches the orthopaedists early, and certainly long before the age of 20 months.

Mr. E. W. Somerville and Mr. J. C. Scott quote an annual figure of 15 cases, from a population of 1,500,000 (*Journal*, March 5, p. 724). If this incidence is applied to England and Wales as a whole (though from my experience I think it is an under-estimate, and that there are probably some more cases in the "pipeline" awaiting diagnosis), then, with an estimated population in England and Wales of about 45,000,000, there should be 450 cases annually. This compares with a total of 914 cases of paralytic polio in England and Wales in 1959. If, therefore, only half the energy and enthusiasm that are at present put into preventing paralytic polio were expended on the early diagnosis of C.D.H., many "headaches" would be avoided.—I am, etc.,

Wembley, Middlesex. R. A. STRANG.

SIR,—In connexion with the last paragraph of the interesting letter of Mr. E. W. Somerville and Mr. J. C. Scott concerning the causation of congenital dislocation of the hip and osteoarthritis in later life (*Journal*, March 5, p. 724), it may be relevant to observe that both these conditions are virtually unknown in those African races where the infant is carried in a sling astride the mother's back, i.e., with hips abducted, for the first year or so of life.

Although there are racial and anatomical differences which may equally well account for the low incidence, it would be interesting to discover whether the European practice of rolling the baby up in a blanket with the legs extended, and then fastening him down in the cot or pram with still more covers, is a factor in the causation of these maldevelopments.—I am, etc.,

London, S.W.16. JOAN BISHOP.

Pitfalls in Chemotherapy of Tuberculosis

SIR,—We were pleased to see that our article (*Journal*, January 16, p. 161) had stimulated some thought and discussion as revealed by subsequent correspondence. We fully endorse the great importance that Dr. Joanna M. Ward (*Journal*, January 30, p. 345) attaches to a close rapport between patient and physician. To establish such a good relationship is certainly the policy of this unit and we believe that of many others. Despite vigorous efforts in this direction, however, we have still found repeated failure to consume P.A.S. (para-aminosalicylate)—often most unexpectedly. Clearly the experience of Dr. N. Wynn-Williams (*Journal*, February 13, p. 498) is similar. It is regretted that Drs. M. O. J. Gibson and M. M. Nagley (*Journal*, February 6, p. 421) clearly misread our references to calcium B-P.A.S. (calcium benzamidosalicylate). They state inaccurately that our condemnation of this drug is based upon no more than two unsuccessfully treated cases. In fact we clearly state in the article that our advice not to use calcium B-P.A.S. is based upon the absence of "rigidly controlled clinical and bacteriological field trials." In addition we indicate reasons for doubting its efficacy; the two cases quoted form only part of this evidence.

We would contest the validity of Dr. Joyce A. Keeping's attempt (*Journal*, February 13, p. 498) to compare the incidence of drug resistance in two clinic areas when there manifestly may be so many variables (e.g., drug-resistance criteria, laboratory methods, clinic practice, type of patient, and population movements). Because it is (rightly) common practice to initiate antituberculosis treatment with streptomycin, P.A.S., and isoniazid, any differences in efficacy between sodium P.A.S. and calcium B-P.A.S. could well be masked; they certainly could not be clearly established without adequate controlled trials. Until positive evidence in favour of calcium B-P.A.S. is produced, we remain firmly of opinion that this drug should not replace sodium P.A.S. Finally may we reiterate that principles of drug usage should be based upon adequate proof of efficacy and not upon individual opinion?—We are, etc.,

GRAHAM POOLE.
PETER STRADLING.

Hammersmith Chest Clinic, London, W.12.

Psychogenic Disorders in Children

SIR,—Dr. J. G. Howells's letter (*Journal*, February 20, p. 567) contains much wishful thinking when he says that "the position should *soon* (italics mine) be reached when there will be an adequate supply of fully trained child psychiatrists." It is the shortage of consultant psychiatric help that has been one of the main reasons for many of our paediatric colleagues attempting, with considerable success, the treatment of the "common minor emotional disorders of children." In Bristol this may have been influenced by the fact that the ratio of psychiatric social worker to psychiatric sessions at the Children's Hospital is at present nineteen to three.

Dr. Howells's main criticisms of Dr. John Apley's scheme (*Journal*, January 16, p. 191) would be, firstly, that paediatricians are enlarging their field of work unjustifiably, and, secondly, that psychiatric social

workers are being given a degree of responsibility which is unwise. Taking the second point first, there is no mention in the article of "diagnosis by psychiatric social workers." The relevant sentence reads, "The psychiatric social worker tries to make friendly contact, and discusses her part in diagnosis and treatment." The tripartite investigation of a child psychiatric case by psychiatrist, psychologist, and psychiatric social worker has long been the accepted practice in child-guidance clinics and many child psychiatric clinics. To suggest that the assessment of the psychopathology of parents is absent from Dr. Apley's plan does scant justice to the experience of Dr. Apley's co-authors who have been engaged for many years in psychiatric social work both in child-guidance and in adult clinics, and in fact their present posts cover both types of work. The opportunity of discussing a particular point with a consultant psychiatrist is therefore readily available. As Dr. Apley points out, one case in five, as a result of the joint conference of paediatrician and psychiatric social worker, is passed on to the full psychiatric team of which the same psychiatric social workers are members, and who, in Bristol, work in the same out-patient department as Dr. Apley. In fact, in 1959, 56% of the cases seen at the psychiatric clinic were referred by consultants in the hospital.

The first point, however, is the more serious one, with its implication that the only doctors fit to treat children's emotional problems are the general practitioner and the consultant child psychiatrist. Child psychiatry is inevitably linked with general practice, paediatrics, and with adult psychiatry: it would be a pity if, while battling for the rights of the general practitioners, Dr. Howells lost sight of the fact that many paediatricians have the requisite personality and experience to allow them to treat minor emotional difficulties, and, at the same time, have enough insight to know when to pass on the more severe cases.—I am, etc.,

Bristol, 8. R. F. BARBOUR.

Asepsis on T.V.

SIR,—I looked in on Dr. Fletcher's television programme dealing with the subject of immunization, relayed on Tuesday, March 8. Now there are many medical and surgical subjects dealt with in this way, and it is probably true to say that most of them depict an aspect of medicine which applies to a minority group in the population. Any inaccuracies in such programmes are rather unimportant provided the main message is adequately dealt with. Immunization, however, is a subject which concerns every member of the community. Such a programme should be especially interesting to parents, for they ought to be knowledged on the detail of immunization so that they understand fully what are its aims; and nowadays, with the need to ensure that adults are protected, for example, against polio, an even wider non-parental group requires education. I must confess to some disappointment, therefore, for the programme did seem to me not only unimaginative but in places confusing.

Had dullness and some confusion been the end of my disappointment I might have been inclined to keep my thoughts to myself. But when in one of the introductory sequences I saw a doctor ejecting the vaccine lymph from the capillary tube on to the child's arm by blowing out the lymph with his mouth, I was really horrified. Such a practice cannot be condemned with too great force, for it implies a complete disregard of the ordinary principles of asepsis and obviously exposes the recipient to hazard. No wonder there are still reports of infection following smallpox vaccination. The use of a rubber teat—even the teat of a baby's feeding-bottle—is so simple that the method is easily learnt. But to see this in a film sequence which had presumably been vetted by its sponsors would suggest that the method of blowing out the lymph is still regarded by some as entirely proper.

This reprehensible practice—one might almost say malpractice—makes one wonder if there is not a need to review the whole detail of the practice of immunization and to instruct the public in what they should expect. It is known, for example, that polio vaccination has been carried out on groups of children by charging the syringe with 10 ml. of vaccine and only changing the needle between each injection. Must one go on being silent about practices which are *known* to be fraught with danger? Is an increased incidence of hepatitis to be the price the public pays for a decreased incidence of polio?—I am, etc.,

Department of Infectious Diseases, Glasgow. THOMAS ANDERSON.

How Morbid Can We Get?

SIR,—May I relate the history of yet another "television casualty"?

An expectant mother aged 28, with a previous history of prenatal hypertension and who knows that her mother "died of blood-pressure," presented at the surgery last evening. She knows that her blood-pressure is higher than it should be (I have not been able to withhold this information from her, as I have had to discuss the possibility of a hospital confinement). She is of good intelligence and of normal emotional stability, so that I was astonished that she should break down emotionally during the course of my examination. On inquiring the cause, she alleged that she had felt very tense and been unable to sleep at night since seeing a programme called "Emergency Ward 10" (which I have not seen), which, according to her description, concerned a woman who had been delivered by caesarean section on account of hypertension, and whom, I gather, had lost her baby.

How morbid can we get?—I am, etc.,

Worthing. A. W. BEATSON.

First Aid

SIR,—In delivering his Hunterian lecture at the Royal College of Surgeons on January 28, Lieutenant-Colonel J. C. Watts, R.A.M.C., said that it was everyone's duty to learn first aid. "Peterborough" of the *Daily Telegraph* drew attention to this and commended it to everyone's attention, and Dame Anne Bryans, deputy chairman of the British Red Cross Society, supported it in a letter to the *Daily Telegraph*, adding that it was the British Red Cross Society's duty to give such instruction.

This commitment to the general public is in addition to the ever-increasing demands to provide training in first-aid for its own members, for the National Hospital Service Reserve, the Civil Defence Corps, industry, and agricultural workers. First-aid courses are arranged by the local branches of the Society in all parts of the United Kingdom, usually in the evenings once a week, but for industry there is also a demand for day-time courses.

The Society would welcome the help of medical officers who are willing to act as lecturers and examiners, and particularly any doctor who could spare time during the day to further this vital work of giving first-aid training to those employed in industry. Doctors who

could give assistance with any of the above courses are asked to communicate with the Medical Adviser, British Red Cross Society, 7, Grosvenor Crescent, London, S.W.1, or with the County Branch Director, B.R.C.S., in their own area.—I am, etc.,

F. C. HILTON-SERGEANT,
Medical Adviser,
British Red Cross Society.

Quiescent Malaria Parasites

SIR,—The possibility that boxers coming to this country from malarious areas are infected by malaria has always been realized by the medical officers of the Boxing Board of Control. Before being granted a licence to box in this country they must undergo a strict medical examination, when particular attention is paid to the splenic area.

However, as a result of the findings of Mr. P. G. Shute in the case he describes (*Journal*, March 5, p. 730), all medical officers of the British Boxing Board of Control were in January last asked to advise all boxers coming to this country from malarious countries to take a course of chloroquine.—I am, etc.,

J. W. GRAHAM,
Administrative Steward and Chairman of Medical Subcommittee,
British Boxing Board of Control.

London, W.1.

Bernard Johnson Memorial

SIR,—The sudden and unexpected death of Bernard Johnson in May, 1959, left the Board of the Faculty of Anaesthetists with a great sense of loss, which became more apparent as the scope of the work he undertook on its behalf came to light. Many of the present activities of the Faculty of Anaesthetists were initiated by Bernard Johnson, and it was his imagination and persistence which carried them through to completion. These include the establishment of the research department, which was not only his idea but for which he collected the funds almost single-handed, the Faculty scientific meetings, the provision of lecture courses, and the training of postgraduate students.

Many of his friends have expressed the wish to have an opportunity to contribute to a memorial, and a committee has been set up to this end. We hope to collect £6,000, and it is proposed that this will be devoted to the foundation of a lecture, the provision of a plaque costing approximately £200 to be placed in the research department of anaesthetics at the Royal College of Surgeons, and to provide for a Faculty adviser in postgraduate studies, a function of the Faculty which was very near to Bernard Johnson's heart.

All those friends and colleagues of Bernard Johnson who would like to be associated with this memorial are invited to send their contributions to the Dean of the Faculty of Anaesthetists, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2. Cheques should be made payable to "The Faculty of Anaesthetists."—We are, etc.

MILES CLIFFORD, Chairman.
GEOFFREY ORGANE, Dean.
T. CECIL GRAY.
J. B. KINROSS.
E. A. PASK.
RONALD WOOLMER.
Bernard Johnson Memorial Committee.

Faculty of Anaesthetists,
Royal College of Surgeons of England,
London, W.C.2.

Obituary

J. B. ALLAN, M.B., Ch.B.Ed.

Dr. J. B. Allan, who practised in Grantham, Lincolnshire, died at his home there on February 11, aged 55.

John Balfour Allan was born at Edinburgh on April 5, 1904, and studied medicine at the university there, graduating M.B., Ch.B. in 1926. After holding various hospital appointments in Edinburgh and Greenock and serving for a time as ship surgeon, he settled in Grantham, joining the late Dr. Frier as partner in 1933. At the time of his death he was the senior member of a partnership of seven doctors. During the second world war he served in the R.N.V.R. as a surgeon-lieutenant for four years. Dr. Allan married the daughter of a Canadian doctor, and she survives him, together with two grown-up children.

F. J. J. writes: Dr. J. B. Allan had a major operation last autumn and with his death at the early age of 55 South Lincolnshire has lost one of its outstanding general practitioners. During his years of service to the community he endeared himself to his many patients. He was indefatigable in the care of the sick and carried an immense burden on his return from service overseas. On the retirement of his senior partner the mantle of clinical authority was automatically assumed by him. He was known for his acumen, which was at times uncanny, his painstaking conscientious care, and untiring search for the truth. He had amassed an immense knowledge of medical data, and had an exceptionally retentive memory. A much esteemed colleague, his breezy humour and confident manner acted as a tonic to an anxious patient and inspired confidence in a worried parent. No trouble was ever too much for him where the interest of the sick was concerned. He held the post of clinical assistant in the maternity department of Grantham Hospital, where he was fully able to display his great obstetric skill and established a tradition which will be difficult to surpass. The nursing personnel were devoted to him. His directness of manner, even to the point of bluntness, was refreshing in its very unusualness. A keen golfer, he had previously been a tennis player, and at both of these sports he excelled.

By his death the profession and district where he practised have lost a doctor who still cherished the ideals of the fast-disappearing older generation but was young enough to absorb and practise all that is better in the new. He will be much missed by a host of grateful patients and by all his colleagues for his devotion to his calling. The sympathy shown by the great congregation at the memorial service and that of his friends may be a measure of solace to his family.

J. H. C. EGLINTON, L.M.S.S.A.

Dr. J. H. C. Eglinton, who was in general practice in Street, Somerset, died at his home there on February 13, at the age of 66.

John Henry Cox Eglinton was born at Street on February 27, 1893, the son of Dr. G. W. Eglinton, and was educated at Rydal and Bristol University, qualifying in 1919. His father had died while he was still a student, and after holding appointments of house-physician and house-surgeon he returned to practice in Street, where he worked for almost forty years, until illness forced him to retire in 1958. From 1939 he was medical officer of health to Street urban district council, and his other appointments included those of medical officer to Butleigh Hospital, appointed factory doctor, medical officer to a large footwear firm, and medical officer to an aeroplane manufacturing company's convalescent home at Ashcott. He also found time to serve

on the Somerset panel committee and was chairman of the West Somerset Division of the B.M.A. from 1935 to 1936 and again in 1946–7. He joined the College of General Practitioners soon after its foundation.

Apart from his medical interests, he was a keen supporter of local sport, playing tennis and cricket for local teams, and being at one time president of the Street cricket and football clubs. A staunch Methodist, he was a valued trustee of his church. His wit enlivened many of the social occasions at which he was a welcome guest.

M. J. F. writes: A wide community will grieve over the loss of "Dr. Jack," who was not only their doctor but a very dear friend. His congenial presence and his generous sympathy heartened the sick and comforted the anxious. The deep appreciation that he had of the troubled mind gave him the rare ability to share the burdens of others, and many will recall how their problems fell into a true perspective under the influence of his warm-hearted spirit. After his children grew up his practice was his only interest, and it was a bitter blow when illness took this from him. He passed his short retirement with a quiet courage and died in that peaceful way that he had so often before wished to others. Our deep sympathy is extended to his widow, who nursed him so tirelessly through many trying months, to his three daughters, and to his son, who is a medical student in Dublin.

PAUL PLAUT, M.D., Ph.D.

Dr. Paul Plaut, who had been a psychiatrist on the staff of the Portman Clinic, died at University College Hospital on January 22, aged 65.

H. H. F. writes: Paul Plaut was born in Berlin, where his father was professor at the Oriental Seminar of the University of Berlin. He studied philosophy, his main interest being in practical psychology, and after obtaining the degree of Ph.D. he was appointed assistant and later associate of the Institute for Applied Psychology in Berlin. Becoming more and more interested in psychopathology, he began to study medicine, qualifying in 1927 and proceeding M.D. in 1928 at the University of Berlin. Then forensic medicine attracted him, and he became "accredited expert" for forensic medicine to law courts in Potsdam and Berlin. He also practised psychotherapy, but did not belong to any of the acknowledged schools.

Having to emigrate in 1938, he came to London and quickly obtained a position at the Institute for the Scientific Treatment of Delinquency (later known as the Portman Clinic). He worked there enthusiastically, particularly during the years of the second world war, and gave his best to the patients, not sparing himself and not taking any holiday for years, when he was the only available psychiatrist at the institute. At the same time he was also responsible for the East London Child Guidance Clinic, when its director, Dr. E. Miller, was away on war service. Plaut continued at the Portman Clinic when it was taken over by the National Health Service and applied his extensive psychiatric knowledge very successfully to the diagnosis and psychotherapy of maladjusted persons and sex deviators. Many people owe their social rehabilitation to his tireless efforts. He retired from the clinic about a year ago on reaching pensionable age.

His health during the last years gave occasional anxiety to his friends, but he would not spare himself. In December, 1959, he suffered what was obviously a coronary attack, but though persistently in pain and feeling ill he refused to go to bed because he wanted to give evidence for a patient in court. He continued work, and only after several days was his wife able to persuade him to seek medical advice.

Paul Plaut was a very cultured man with wide interests; he was a tireless worker and, particularly in his younger years, a prolific writer. He wrote seven books. His *Psychologie der produktiven Persoenlichkeit* is possibly his best known; his last one, written after retirement from the Portman Clinic, *The Sexual Offender and His Personality*, is just in the press. He also wrote many papers on all sorts of problems of normal and pathological psychology. His interests changed from more general questions, such as the psychology of art, of culture, and of history, to problems of a more individual nature—the psychology of the productive person, of the witness, of the criminal. In parallel with this he turned more and more from literary to practical medical work and the number of his publications decreased. Often concealing his warm-hearted personality behind a somewhat sardonic wit, he enjoyed a sharp debate. He liked to talk, but his was also the gift of patient and attentive listening. He was a solicitous and devoted husband and father. To his widow and to his daughter we offer our sincere sympathy.

J. R. BOYD, C.B.E., *M.C.*, M.D., F.R.C.P.Ed. F.R.A.C.P.

Dr. J. R. Boyd, a distinguished New Zealand physician, died in Wellington on January 31, aged 73.

James Roberts Boyd was born at Innerleithen, Peeblesshire, on September 6, 1886, the son of the Rev. James Boyd, and studied medicine at Edinburgh University, graduating M.B., Ch.B. in 1911, and proceeding M.D. in 1914. After resident appointments in Edinburgh Royal Infirmary he joined the Colonial Medical Service and was posted to Fiji in 1913. During the first world war he served as a captain in the R.A.M.C. and with the mounted division of the New Zealand Forces in Mesopotamia, where he was awarded the Military Cross. After the war Dr. Boyd returned to New Zealand and practised in Taranaki.

In 1924 he went to Wellington as a consulting physician, being one of the first physicians in New Zealand to practise solely as a consultant. In 1923 he became M.R.C.P. of Edinburgh and in 1938 was elected a Fellow. He was elected a foundation Fellow of the Royal Australasian College of Physicians in 1939. From 1933 to 1946 he was the first senior physician at Wellington Hospital. During the second world war Dr. Boyd was a medical consultant to the New Zealand Forces and was appointed C.B.E. In 1954 his colleagues established the James Roberts Boyd prize fund in recognition of his outstanding service in peace and war. He was honorary physician to a former Governor-General, Lord Freyberg, V.C., and a medical adviser to the Royal Party during the 1954 visit. He is survived by his wife.

W. L. BROWN, M.B., C.M.

Dr. W. L. Brown, who formerly practised first at Shildon in Co. Durham and then at Hinderwell in Yorkshire, died at Whitby on January 12 in his 90th year.

William Limont Brown was born at Partick, Glasgow, on May 1, 1870, and educated at Glasgow High School. For the rest of his life he followed the successes and failings of his old school in the rugby football world, and was always proud of its achievements. He was a medical student at Glasgow University, graduating M.B., C.M. (with commendation) in 1892. After working for a time as clinical clerk at Gartnavel Asylum he took an assistantship with Dr. Davison at Newburn-on-Tyne. Two years later he bought a practice at Shildon, Co. Durham, and in 1900 he married Miss Mary Kirton. Among other activities at Shildon he was a member of the urban district council and of the Bishop Auckland board of guardians. For some years he was medical officer of health for Shildon, and when he moved in 1927 to Hinderwell, where he bought a practice for himself and his daughter, Dr. Dorothy Brown, he became medical officer of health for that district. In 1937 he retired from general practice and went to live at Whitby.

E. F. B. writes: Dr. W. L. Brown was a man with a somewhat gruff exterior, beneath which lay a charm and sense of humour which endeared him to all. He took a keen interest in all outdoor sports at Whitby and was a member of all the athletic clubs. In a letter which I have

before me, and which was written since his death by the doctor to whom he handed over his practice in Shildon and who has himself just retired from practice, I quote the following: "I have always had a great regard for W. L. B. ever since the days when we tramped round Shildon together and he showed me the real old-style family doctor at work, a class now, I fear, that has passed into the limbo of forgotten things." Although I only knew him for some twenty-five years, I knew him as a kindly man. The people of Whitby miss his familiar figure taking his fox-terrier for a walk, and the medical profession of this country has lost yet another of those who were the backbone of medicine before nationalization destroyed, to a very large extent, the mutual trust, friendship, and respect that used to exist between the family doctor and his patient.

RONALD FARNCOMBE, M.R.C.S., L.R.C.P.

Dr. Ronald Farncombe, who had practised in Bexhill for twenty-four years, died suddenly at his home there on January 15. He was 53 years of age.

Ronald Farncombe was born on December 11, 1906, and after schooling in Brighton he studied medicine at St. George's Hospital, qualifying in 1934. After holding resident appointments at St. Mary Abbots Hospital and at the Hammersmith Hospital (British Postgraduate Medical School) he went into general practice in Bexhill in 1935. During the second world war he served in the R.A.M.C. at home, not being fit for service overseas. He had a lifelong interest in the St. John Ambulance Brigade, joining as a private at the age of 14, proceeding through all the ranks, and eventually holding the offices of divisional surgeon for Bexhill and county surgeon for East Sussex. For a time he was a member of the Hastings group hospital management committee and of the house committee of the Bexhill Hospital and also of Darvell Hall Sanatorium.

J. H. D. writes: Ronald Farncombe was a kind, quiet, and very conscientious practitioner, concerned only with the welfare of his patients. After eighteen years of single-handed practice he took in a junior partner and shortly afterwards amalgamated with my firm (a logical step, as we had frequently looked after each other's patients), and we had six pleasant years working together. Apart from his work his passionate interest was in the designing and making of gardens. Our sympathy goes out to his widow, son, and two daughters.

P. G. MURPHY-O'CONNOR, M.B., B.Ch.

Dr. P. G. Murphy-O'Connor, who was in general practice in Reading for 39 years, died at his home in that town on January 17. He was 68 years of age.

Patrick George Murphy-O'Connor was born in Cork in 1891 and was educated at Cork University, graduating M.B., B.Ch. in 1914. He came from a family of nine children, three of the sons becoming doctors, three priests, and one sister a nun. An Irish rugby trialist, he captained teams from Munster, Berkshire, and the University of Cork. He also represented Cork University in the 100 yards sprint. For 35 years he accompanied the annual national pilgrimage from England to Lourdes as one of the medical team caring for the sick, and for 40 years he was president of the Reading branch of the Society of St. Vincent de Paul, which looked after the needs of the local Catholic poor. For these services he was made a Papal Knight of the Order of St. Gregory.

In 1924 he married Ellen Teresa Cuddigan, from Cloyne, Co. Cork, and by her he had five sons and one daughter. Three of his sons are priests and one, James, a doctor, played rugby for Ireland against England at Twickenham in 1954, thus carrying on the family tradition in sport.

George Murphy-O'Connor fought the good fight and kept the faith—a truly "gentil knight." To his widow and family we express our sympathy.—N. C. H.

E. P. IRVING, M.B., Ch.B.

Dr. E. P. Irving, who was formerly in practice in Burslem, Staffordshire, died recently at the age of 65.

Edward Porteous Irving was born at Chester on March 2, 1894, and studied medicine at Glasgow University, graduating M.B., Ch.B. in 1917. Immediately joining the R.A.M.C., he served for three years in India and Persia. When he returned to civilian life he held house appointments at Southport Infirmary, Mansfield and District Hospital, and the Central London Throat, Nose, and Ear Hospital. After practising for some time in Chester, Dr. Irving decided to settle in the Potteries, and in 1932 joined Dr. John Hallam in a partnership in Burslem. He remained there until 1950, when he went into semi-retirement, joining the part-time staff of the Ministry of Pensions and National Insurance. He also undertook some industrial medical work and a little private practice. During the time he was in the Potteries he took part in many of the social activities of the district, and was president of the Fenton Bowling Club.

J. H. writes: Not sparing himself in his professional duties, Dr. Irving was indeed the ideal physician, beloved of his patients, to whom he became not only medical adviser but friend. To his patients his retirement caused a sense of loss which was intensified by his sad passing. I remember him with affection as a most helpful and loyal colleague and as a faithful, trusted, and valued friend, for whose passing his professional colleagues, all of whom will wish to associate themselves with this tribute, must remain the poorer.

O. THOMAS-JONES, M.B.E., L.R.C.P.&S.Ed.

Dr. O. Thomas-Jones died at his home at Colwyn Bay on February 9. He was 83 years of age.

Owen Thomas-Jones was born at Cemaes Bay, Anglesey, on May 5, 1877. He had a full and, in many ways, unique life, beginning his medical career at the age of 16 as an unqualified assistant to Dr. Grey Edwards of Bangor, and filling similar posts in Llanfairtalhaiarn and Llanberis. He was an excellent horseman, which was a help to him in visiting patients in the Welsh mountains. This ability also stood him in good stead when, during the South African war, he enlisted with the Imperial Yeomanry (Rough Riders). He did not stay long with this unit, but was soon given command of a body of native scouts. He finished the war with the rank of captain, and with his gratuity and the money he had saved returned to his first love, medicine, studying at the Universities of Glasgow and Edinburgh and qualifying in 1906. He started practice in Blaenau Ffestiniog, where he married Miss Morfydd Thoms, the daughter of another doctor. In 1914 he went to Barry, where, during the first world war, he was in charge of a base hospital, later being appointed M.B.E. In 1928 he came to Colwyn, with the intention of semi-retirement, but his popularity increased, so that he had to take a partner.

His death marks the passing of a generous friend and a loyal colleague, and also the passing of an era—G. J.

JANE L. J. BIRKETT, M.D.

Dr. Jane L. J. Birkett (née Haskew), formerly a medical missionary in India, died at her home at Weston-super-Mare on February 21 at the age of 94.

Jane Louisa Jarrett Haskew was born in Calcutta on May 8, 1865, the eldest of 11 children, and studied medicine at the London (Royal Free Hospital) School of Medicine for Women, qualifying in 1887 and proceeding to the M.D. (Brussels) a year later. She immediately returned to India to work for the Zenana Bible and Medical Missions at the

Kinnaird Memorial Hospital in Lucknow. In 1899 she married the Rev. A. I. Birkett of the Church Missionary Society, Lucknow. A year later she and her husband went to work among the Bhils in Rajputana, where famine was rife. Dr. Birkett laid the foundations of a modern medical service in the area, establishing a small hospital and travelling far and wide. In 1916 her husband died, and she returned to England, her ship being torpedoed in the Mediterranean. In 1919 she returned to her medical missionary work with the Bhil Mission of the Church Missionary Society. Retiring in 1922, she came to live with her two daughters in Weston-super-Mare, where she continued in good works, helping many by her gentleness, wisdom, patience, and sympathy. She is survived by her daughters, one of whom is a medical missionary.

K. G. PANDALAI, M.B., C.M., F.R.C.S.

Colonel K. G. Pandalai, formerly of the Indian Medical Service, died at Madras on February 5, aged 74.

Krishnan Gopinath Pandalai was born on May 20, 1885. He studied medicine at Madras, graduating M.B. in 1909. Two years later he qualified M.R.C.S., L.R.C.P. from the Middlesex Hospital, London. He obtained the F.R.C.S. of England in 1921.

A. S. M. N. writes: Colonel Pandalai, on reversion to the civil side of the Indian Medical Service after the first world war, was posted to Madras district as professor of surgery at the Madras Medical College and superintendent and surgeon to the Government General Hospital. On his retirement, as a consultant surgeon with a modern nursing-home he played a very prominent part in the medical life of Madras for well over a quarter of a century. In all these capacities he discharged his duties with conspicuous ability. He was the founder president of the Indian Association of Surgeons. Having built up a large practice, he rendered a notable service to the public of Madras and was liked and respected by everyone who knew him.

Medico-Legal

DRUNKEN DRIVING

[FROM OUR LEGAL CORRESPONDENT]

A grave case of drunken Christmas Eve driving was the subject of criminal proceedings at the Old Bailey on March 3 (*The Times*, March 4). George Victor Bye, aged 28, an upholsterer of Wandsworth, pleaded guilty to driving under the influence of drink on December 24 and causing the death of a woman pedestrian. He was sentenced to three years' imprisonment and disqualified from driving for 10 years.

On Christmas Eve, Bye's employers provided the staff with beer, whisky, rum, and apricot brandy. When Bye left for home in his car he was very drunk. On his journey he hit two vehicles and failed to stop, but later mounted the grass verge at right angles to the road. One of the vehicles which had been hit drew up in front to stop him proceeding, but Bye got round it and proceeded on his journey. He then took a bend on the wrong side in face of oncoming traffic, mounted an island in the middle of the road, smashed "every bone" in the body of an elderly woman standing there, and continued for 124 ft. on the wrong side of the road with her on his bonnet. Having dismounted, he asked, "Have I hurt her?" At the police station he said, "I am quite drunk, I don't want a doctor."

For the defence it was stated that Bye was suffering from a thyroid condition for which he had recently undergone an operation, and which made him unusually susceptible to drink.

Medical Notes in Parliament

QUESTIONS IN THE COMMONS

No Date for Talks on Pay Report

Mr. L. PAVITT (Willesden, West, Lab.) asked the Minister of Health on March 11 whether he would fix a date for preliminary general discussions with the medical profession concerning the report of the Royal Commission on Doctors' and Dentists' Remuneration.

Mr. D. WALKER-SMITH: I am not yet ready to propose a date, but I have informed the profession that the Secretary of State for Scotland and I would wish to have such discussions as soon as the Government have completed their initial study of the Report.

Poliomyelitis Vaccination

Colonel TUFTON BEAMISH (Lewes, Con.) was told by Mr. WALKER-SMITH that about £6 million had so far been spent on the purchase of poliomyelitis vaccine for England and Wales, and the further cost of supplies for 1960 is estimated to be about £1.7 million. Expenditure incurred by local health authorities could not be separately calculated.

Mr. R. RUSSELL (Wembley, South, Con.) asked the Minister if he was aware that an oral vaccine against poliomyelitis had been developed in the Union of South Africa; and what were the prospects of its being available for use in Great Britain. Mr. WALKER-SMITH replied that decisions regarding the use in this country of oral poliomyelitis vaccine from any source must await the results of the Medical Research Council's trials.

Road Accident Statistics

Mr. JOHN HARVEY (Walthamstow, East, Con.) asked the Minister of Transport on March 9 if he would explain the circumstances under which road accidents were designated in the published statistics as being due to drink; and whether he was satisfied that the present system gave an accurate reflection of the number of accidents in which the consumption of alcohol might have been a contributory factor. Mr. ERNEST MARPLES stated that the statistics reflected every instance of a driver or cyclist involved in a fatal or serious accident who had appeared to the police to be in such a condition as to have rendered him liable to be charged with a drink offence under the Road Traffic Acts. The offence might be cycling, or driving or being in charge of a motor vehicle, in either case while under the influence of drink to such an extent as to be incapable of having proper control of the vehicle. He was sure that drink and other hidden factors contributed to many more accidents than the statistics showed, or indeed than it would be practicable for any reporting or investigating system to reveal.

Mr. HARVEY said that a variety of arguments were being advanced by various interests, and the greater clarification that could be given by the Ministry the better it would be for all concerned. Mr. MARPLES agreed. The size of his postbag, he said, showed the variety of causes to which people attributed accidents. In considering the effect of drink he was sure that the best thing had been done by giving the information about Christmas accidents to the Road Research Laboratory and asking for a painstaking investigation and a scientific analysis. It was wrong to proceed by "hunches."

BRAIN-WASHING TECHNIQUES

The Secretary of State for War, Mr. CHRISTOPHER SOAMES, faced questions on brain-washing from three members of the Opposition on March 9, as a consequence of a discourse

on this subject at the Royal Institution on February 26 by Professor ALEXANDER KENNEDY, professor of psychiatry at Edinburgh University. Mr. E. THORNTON (Farnworth, Lab.) asked Mr. Soames what use was made by the Army of brain-washing techniques on prisoners during the last war; if he would describe the techniques employed; and the last date on which they were used. Mrs. BARBARA CASTLE (Blackburn, Lab.) asked if he had studied the technique of brain-washing, used to extract confessions, described by Professor Alexander Kennedy in his recent lecture to the Royal Institution; to what extent this technique had been used in the Army since the end of the war; and for a statement. And Mr. M. LIPTON (Brixton, Lab.) asked what instruction in brain-washing techniques was now given to Army personnel.

Mr. SOAMES: The Army has never made use of the techniques described by Professor Kennedy. No military organization exists, or has existed, to carry out such a task.

Professor Kennedy's Letter

Mr. THORNTON asked Mr. Soames if he had carefully studied Professor Alexander Kennedy's discourse to the Royal Institution? If he had, he must feel that now the whole world had conclusive proof that these brain-washing techniques were used to extract confessions. Had not we in this country been led to believe that these pernicious brain-washing techniques were the monopoly of the totalitarian Powers? Was he aware of the world-wide concern there would be if it was found that there was not here a difference of principle but merely of degree? Would the Minister consult his colleagues so that a full statement on this matter, this very important principle, could be made to the House at an early date? Mr. SOAMES said he could assure Mr. Thornton that these techniques had never been used in this country and that Professor Kennedy had never said they had. He had been in touch with Professor Kennedy and had a letter from him, extracts from which he should like to read:

"I have looked at the script used by me at my discourse at the Royal Institution and can give you full assurance that at no point in the script or in the discourse itself did I make any reference to Britain or to any sort of interrogation or brain-washing activities carried out there. As there were about four hundred people present it would not be difficult to obtain confirmation of this. My references to brain-washing were entirely general, and no Government was referred to. My account of its principles could be deduced entirely from material already available in books and magazines. As I spent four and a half years in the Middle East during the war it is unlikely that I would know anything about secret activities in Britain."

He went on to say:

"I was naturally annoyed when I saw the headline in the *Observer*, but I realized that no good is ever done by complaining about inaccuracies in newspapers, so I took no action."

Mrs. CASTLE asked if they were to deduce from that reply that it was only the British Government that Professor Kennedy was now exonerating from complicity in these methods? Did not the Minister agree that the allegations made were of sufficient seriousness to warrant this matter being cleared up very thoroughly? Was Professor Kennedy referring to any other allied Government, or to what was he referring?

Mr. SPEAKER: Order. The Minister cannot be asked about activities for which he is not responsible.

Article in "Daily Mail"

Mr. LIPTON said he was not concerned with what Professor Kennedy had said, or with what happened years ago. What kind of instruction was being given now? He asked that in view of the rather alarming disclosures in that morning's issue of the *Daily Mail*. As it was quite impossible to clear this matter up by an argy-bargy across the floor of the House, would Mr. Soames arrange for interested members to pay a visit to the depot of the Intelligence Corps, somewhere in Sussex, so that they could see for themselves what kind of training was given there, and what was happening? Mr. SOAMES replied that what Professor Kennedy had been talking about in his lecture and the article in the *Daily Mail* were entirely different matters. But he was very glad to have this opportunity of saying categorically that the sort of methods which were referred to in the *Daily Mail* article had never been used by the British Army upon its prisoners, and they never would be used. The fact remained, however, that other countries did use these methods, and there were certain troops—particularly our spearhead troops, such as the Parachute Regiment and the S.A.S.—the nature of whose job made them more liable to capture and also placed them in possession of information which would be very valuable to an enemy. It was of the greatest importance that they should be taught the sort of treatment to which they might be subjected if they were captured—as many of our troops in Korea were subjected—so that they might be able the better to withstand it.

Application in Geriatrics

Mr. G. WIGG (Dudley, Lab.) said that Professor Kennedy had had a distinguished career as a soldier, and that his reputation as a psychologist and psychiatrist was international in character. His lecture at the Royal Institution was only scientific in character and a great deal of it was designed to show the relationship between brain-washing techniques and the possibility of curing delirium in the aged. With the Speaker's permission, he would add that if Professor Kennedy had given his assurance to the Minister the House could accept that assurance without any hesitation whatever. Mr. SOAMES thanked Mr. Wigg. He absolutely agreed with what Mr. Wigg had said about Professor Kennedy's lecture.

Mr. F. J. BELLENGER (Bassetlaw, Lab.) said that, although the House would, of course, accept what Mr. Soames had said as being said in all honesty and sincerity, had he not looked at the *Daily Mail* article which alleged that answers were given to the newspaper's questions by a representative of the War Office? Had he better not look at his own public relations department? Mr. SOAMES: "I have certainly looked at the article. Those concerned were asked specific questions about whether we gave our troops this training. The answer is, 'Yes, we do'—and it is right and proper that we should."

ADMISSION OF HANDICAPPED REFUGEES

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Revised criteria for the admission to the United Kingdom of handicapped refugees have been settled in consultation with the United Kingdom Committee of the World Refugee Year. Mr. D. RENTON, Under-Secretary at the Home Office, announced on March 10 that lists of applicants among refugees of long standing would be prepared on the new basis, and consideration would then be given to the numbers who could be admitted, in the light of offers of sponsorship received by the voluntary bodies concerned.

Criteria for Selection

After Easter a British team will visit Germany, and if necessary Austria and Italy, to interview refugees and their families who have proved difficult to resettle in those countries. Regard will be paid to the probabilities of the family becoming self-supporting within a reasonable period, but families containing an incurable or permanently handicapped member will not be ruled out; a limited number which include a sick breadwinner will also be accepted.

To qualify for selection a refugee must have been difficult to resettle and be a physically or socially handicapped person, or a member of a family which includes such a person. "Physically handicapped" means for this purpose (*a*) suffering or has suffered from curable tuberculosis or other curable illness which has hitherto been a bar to emigration; (*b*) suffering from other physical defect—e.g., loss of a limb, deafness, partial loss of sight, but capable of becoming self-supporting; or suffering from some incurable disability but can be cared for by other members of the family and not in need of hospital care.

RADIOACTIVE SUBSTANCES REDEFINED

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The Radioactive Substances Bill, to which the House of Commons gave a second reading on March 8, differs in one important respect from the measure as it was introduced in the House of Lords. Radioactive substances and waste were there defined in the interpretation clause (18) in terms relating radioactivity to processing. These sections are now replaced by a new clause in which radioactive material and waste are related to a list of specified elements enumerated in a new Schedule. The nine elements specified are actinium, lead, polonium, potassium, protoactinium, radium, radon, thorium, and uranium; and to each there is attached what concentration of radioactive substance it must contain—in its solid, liquid, or gaseous form—before it is to be regarded as "radioactive material" for the purposes of the Bill. It was explained when this change was made that the concentrations specified are about one-tenth of those which informed opinion regarded as capable of being ingested for a lifetime without harm; and that they took into account the fact that the International Commission on Radiological Protection was likely to publish revised maximum permissible levels soon. The schedule can be amended if other naturally radioactive materials come into common use or new knowledge makes some alteration of the limits of concentration desirable.

In the light of this change it was interesting to hear the Minister of Housing and Local Government tell the Commons that in this Bill the Government were setting minimum standards; that the system of control (he was speaking in the context of consultation with local and public authorities) must be watched; and that they must be prepared to consider amending Bills as scientific knowledge and practical experience grew. He adopted the same approach towards the national disposal service which for two years the Atomic Energy Authority is to provide as agents for the Government. Those two years would afford an opportunity to see what was the best plan for the future. The Bill is, in its purpose, an agreed measure, and goes to a standing committee with that advantage.

Vital Statistics

Fatal Road Accidents

Deaths due to road accidents in England and Wales in January numbered 507. This was 37 more than in January, 1958, and 126 (or one-third) more than in January, 1959, when there was an unaccountable fall in road deaths. Road traffic as a whole increased by about 13% between January, 1959, and January, 1960. Of those who were killed, 243 (21 children and 222 adults) were pedestrians, 49 pedal cyclists, 7 "moped" riders, 12 motor-scooter riders or passengers, 70 motor-cycle riders or passengers, and 126 other motorists or passengers. Of the 1,211 motor-cycle drivers involved in fatal and serious accidents, 197 were learner drivers. Among pedestrians killed when crossing the road, the largest numbers were in the age-groups 5–9 and 70 and over.

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available

	Week Ending Feb. 27	Week Ending Mar. 5
Measles		
Kent	209	297
Ashford U.D.	94	189
Lancashire	459	565
Blackpool C.B.	52	88
Liverpool C.B.	78	136
Yorkshire North Riding	71	116
Middlesbrough C.B.	58	103
Dysentery		
Durham	29	63
Jarrow M.B.	8	39
Stanley U.D.	3	10
Essex	107	111
Epping and Ongar R.D.	0	16
Lancashire	458	451
Liverpool C.B.	42	52
Oldham C.B.	98	63
Preston C.B.	28	30
Ashton-under-Lyne M.B.	32	44
Radcliffe M.B.	7	23
Swinton and Pendlebury M.B.	37	29
Preston R.D.	7	27
London	177	203
Islington	22	26
Southwark	29	43
Surrey	15	30
Sutton and Cheam M.B.	1	14
Wiltshire	33	46
Swindon M.B.	20	19
Cricklade and Wootton Bassett R.D.	9	20
Yorkshire West Riding	126	114
Sheffield C.B.	38	39
Glamorganshire	25	52
Ogmore and Garw U.D.	12	32
Food-poisoning		
London	29	50
Wandsworth	18	35
Essex	13	71
Thurrock U.D.	3	30
Romford M.B.	1	14
Ilford M.B.	2	12
Warwickshire	13	43
Birmingham C.B.	9	41

Stillbirths in Scotland

A special analysis of stillbirths during the 20 years 1939–58 is given in the latest *Annual Report of the Registrar-General for Scotland* (No. 104, 1958, H.M.S.O., 25s.). It shows that in general the stillbirth rate increases with increasing age of mother, and, independently, with increasing parity. An important exception is that the rate is unusually high in first births. For women aged 40 and over the rate is about 50% higher than for women aged 35–39.

Over the 20 years the stillbirth rate has been halved from about 42 per thousand total births to about 23. A large reduction in the rate is reported for each maternal age group. The largest reduction was for mothers aged 30–34, for whom the rate fell from 46 in 1939 to 24 in 1958. For mothers under 25 the rate fell from about 30 to about 20; for those aged 40–44 the rate fell from 74 to 49.

In 1958 there were 2,324 stillbirths, of which the sex was as follows: male 1,176, female 1,147 (and 1 unstated). Of these 538 were attributed to foetal defects, 434 to other placental and cord conditions, 397 to ill-defined causes, 343 to antepartum haemorrhage, 239 to difficult labour, and

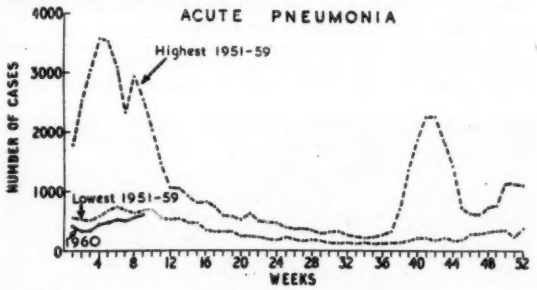
210 to toxaemias of pregnancy. Of stillbirths due to congenital defect, four-fifths were caused by anencephalus and hydrocephalus.

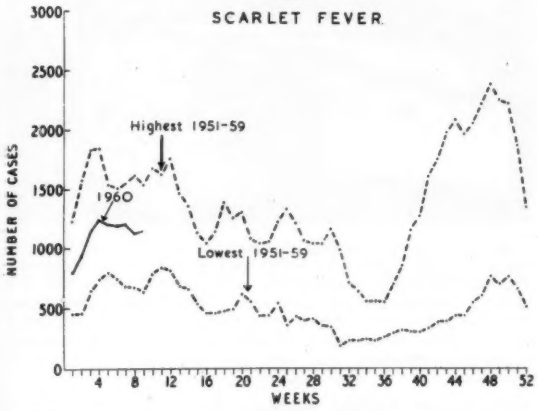
Influenza in England and Wales

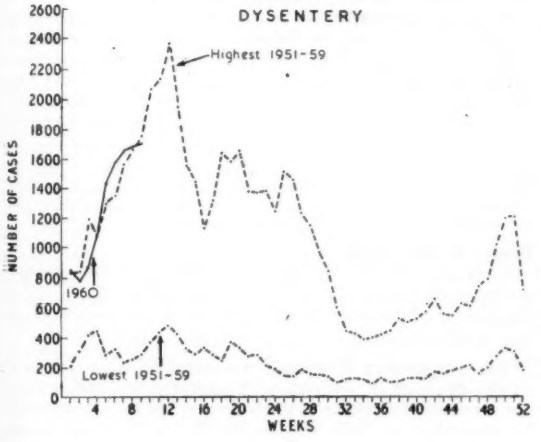
The deaths from influenza fell to 42 in the week ending March 5, having been ten more in the previous week. Both notifications of pneumonia (596) and deaths (859) were slightly up on the previous week, but deaths from bronchitis (766) were over 100 fewer. At 209,044 the weekly new claims on the Ministry of Pensions and National Insurance were 180,000 fewer than in the same week in 1959.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus ------, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 27** (No. 8) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	0	0	1	2	5	0	4	0	3
Dysentery	1,667	177	238	32	3	1,049	67	122	14	8
Encephalitis, acute	3	0	2	0		1	1		0	
Enteric fever:										
Typhoid	0	0	0	0	3	2	0	0	0	
Paratyphoid	4	0	0	0		11	1	0	0	
Food-poisoning	146	29	7	0		148	13	6	0	
Infective enteritis or diarrhoea under 2 years				13	16				6	28
Measles*	2,131	60	54	3	56	24,951	1419	868	584	988
Meningococcal infection	20	2				35	4	21	0	
Ophthalmia neonatorum	16	1	5	0		29	10	6	0	
Pneumonia†	550	36	237	7	5	2,926	276	762	26	16
Poliomyelitis, acute:										
Paralytic	1	0	0	0	4	7	0	0	0	
Non-paralytic	3	1	2			2	0	0		
Puerperal fever§	192	35	10	2	1	309	41	22	0	
Scarlet fever	1,126	44	73	39	14	1,207	55	78	35	20
Tuberculosis:										
Respiratory	432	62	66	13		476	61	87	13	
Non-respiratory	57	1	8	2		53	8	12	6	
Whooping-cough	856	82	174	5	51	589	23	51	77	117

DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		2	0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0	0		1	0	0	0	
Infective enteritis or diarrhoea under 2 years		0	1	0	2	10	0	3	0	0
Influenza	56	5	0	0	0	1,571	163	57	4	4
Measles	-	0	0	0	0		0	0	0	2
Meningococcal infection		0	1				1	1		
Pneumonia	820	52	44	27	7	2,121	244	95	21	18
Poliomyelitis, acute	0	0		0	0	0	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	88	11	9	0	8	143	15	16	1	2
Non-respiratory		2	0	0	0		1	0	0	1
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	368	29	41	10	10	410	38	39	13	17
Deaths (excluding stillbirths)	12,520	967	794	184	186	17,340	1717	1028	161	213
LIVE BIRTHS	15,461	1315	1069	280	373	15,593	1272	1014	265	373
STILLBIRTHS	346	32	28			327	21	25		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Sale of "Imferon" Suspended

A leading article in the *British Medical Journal* of March 12, reviewing the evidence of the carcinogenic effect of "imferon" in experimental animals, concluded that "the existing evidence is certainly sufficient to warrant, and indeed to demand, its speedy withdrawal from any kind of general use in man."

Benger Laboratories, Ltd., issued on March 15 the following statement to the press (*The Times*, March 16):

In the interests of large numbers of patients all over the world who have been treated with Imferon, Benger Laboratories Ltd. issue the following statement:—

An article has appeared in the medical Press stating that there is a possibility of cancer being caused by the administration of this drug. Benger Laboratories point out that this statement is based exclusively on experiments with mice and rats. No evidence is offered that the results apply to man.

Scientists at Benger Laboratories have been carrying out experiments with this drug for seven years and are satisfied that in clinical practice the drug is harmless.

Over a period of six years more than one million patients are estimated to have been treated with this drug. It is widely recognized as a highly effective treatment for iron deficiency. About 100 published scientific papers pay tribute to its value.

As far as Benger Laboratories know, there has never been any evidence of cancer developing in man by the use of this drug. It is their opinion, shared by many experts, that those patients who have received Imferon at any time need have no fear of cancer as a result.

Nevertheless, in view of the alarm which has been created, the manufacturers have felt it their duty to inform the Ministry of Health that they have decided to suspend the sale of the drug for general use, pending an independent re-examination of all the available evidence.

Guide to Mental Health Act

The "Practitioners' Guide to the Mental Health Act, 1959," which appeared in the Christmas issue of the *B.M.J.*, is being reprinted as a handy pocket booklet. This is in response to a very large demand from medical officers of health and general practitioners. Those who have ordered copies will receive them shortly. Others can obtain the "Guide" (price 6d. a copy, post free) on application to the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

M.R.C. Nathan Trust Research Fellowship

The Medical Research Council invite applications for a Research Fellowship, tenable in the United Kingdom, provided by the Nathan Trust. This appointment is being made under the auspices of a special committee set up by the Council for the evaluation of different forms of therapy in bone sarcoma. Applications, giving a full *curriculum vitae*, a list of publications, and the names of two referees (two signed testimonials in the case of candidates overseas) should be sent to the Secretary of the Council, 38, Old Queen Street, Westminster, S.W.1., by April 30.

Candidates should be clinically experienced British medical graduates who should preferably have some knowledge of research methods in clinical medicine, surgery, pathology, or radiology; and should be willing to engage in this investigation for at least two, or possibly three, years, if the progress of the research should so require. The Fellowship will provide a salary of £1,500 to £2,000 a year according to age and experience, with superannuation provision in addition; the appointment will be made for one year in the first instance, but is renewable for up to three years subject to satisfactory progress.

Hospital Board Chairmen

Three new chairmen of Boards of Governors have been appointed in London. They are Mr. M. W. PERRIN (St. Bartholomew's Hospital), Mr. H. R. MOORE (London Hospital), and Sir REGINALD HOLMES WILSON (Hospitals for Diseases of the Chest).

Mr. Perrin is chairman of the Wellcome Foundation Ltd., and also of the Institute of Cardiology in the University of London. Mr. Moore has for many years been a member of the Board of Governors of the London Hospital, of which he was deputy chairman. Sir Reginald Wilson has had long experience in public administration and is a member of the British Transport Commission.

Langley Prize

The London School of Hygiene and Tropical Medicine announces that the Langley Prize has been awarded to Dr. DAVID SCOTT, epidemiologist in the medical service of Ghana, for his paper on "The Epidemiology of Human Trypanosomiasis in Ashanti, Ghana."

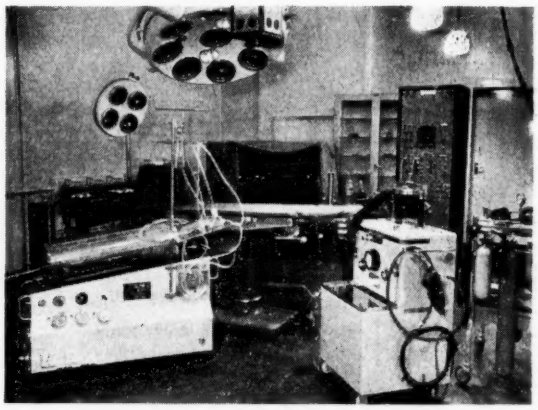
Proposed Night Help Service

A report by the Health Committee of the County Borough of Wolverhampton has been adopted. It recommends the introduction on a limited scale of a service to relieve relatives of those who are ill of some night duties, and to provide night help for the unattended sick.

Glasgow Royal Infirmary

A clinical department for cardiovascular surgery—constituting a meeting-ground for the disciplines of medicine, radiology, biochemistry, and surgery—was officially opened at Glasgow Royal Infirmary on February 26.

The department has 12 beds and extensive and highly developed ancillary services. The operating theatre, shown here, is equipped with the most modern devices in cardiac surgery, is fully screened



to minimize electrical interference with the recording and monitoring unit, and, together with the *x*-ray room, is air-conditioned. The equipment for cleansing and sterilizing surgical instruments includes an ultrasonic cleaner and a high-pressure, high-speed instrument autoclave. There are a large anaesthetic room and a recovery room, and, linked with the cardiosurgical department, a small biochemical unit with four additional beds and a laboratory.

Anglo-French Medical Exchange Bursaries

Bursaries, offered by the Institut National d'Hygiène and tenable in France, will be awarded in May to young British medical men engaged in clinical or experimental medicine or in biological research. Application forms can be obtained from the Director, The Ciba Foundation, 41, Portland Place, London, W.1. The closing date is April 21.

The bursaries will be tenable at any hospital or research institute in France and can be held during the current calendar year or the early part of 1961. The value of the grants is 870 N.F. (about £63) a month, tax free. Awards will normally be made for periods of between two and four months.

People in the News

Professor H. P. GILDING, professor of physiology, Birmingham University, is visiting Pakistan in the spring at the request of the Pakistan Government to advise on medical and medical educational services there.

Mr. SOMERVILLE HASTINGS was installed as a Freeman of the Borough of Barking at a ceremony on January 22. He represented Barking in Parliament from July, 1945, until his retirement in 1959, and during his career in the House

he introduced a Private Member's Bill which led to the Hypnosis Act of 1952 banning demonstrations of hypnosis as stage entertainment.

Brigadier J. E. SNOW, late R.A.M.C., has been appointed honorary surgeon to the Queen from December 3 last.

Mr. TERENCE CAWTHORNE is to be the guest of honour of the American Laryngological, Rhinological, and Otological Society at their annual meeting in Miami.

Professor J. MCMICHAEL, F.R.S., left on March 13 for the Sims Professorial tour of Australia and New Zealand, and will be away until July.

COMING EVENTS

Conference on Industrial Health.—March 24, 10.30 a.m.–5.15 p.m., B.M.A. Scottish House, 7, Drumsheugh Gardens, Edinburgh, 3 (off Queensferry Street). Details from Industrial Welfare Society, 48, Bryanston Square, London, W.1.

Auxiliary Royal Army Medical Corps Funds.—Annual general meeting, April 4, 5 p.m., 11, Chandos Street, London, W.1.

N.W. England Faculty, College of General Practitioners.—Symposium: "Chronic Bronchitis in General Practice," 2 p.m., April 10, Midland Hotel, Manchester. Details from Dr. S. FREEMAN, 1080, Stockport Road, Levenshulme, Manchester, 19.

Refresher Course in Psychological Medicine.—A series of 11 weekly lecture-seminars, starting April 27 or 28, on "Aspects of Psychological Medicine of Interest to General Practitioners" has been arranged under the auspices of the British Postgraduate Medical Federation by the Department of Psychological Medicine, Royal Free Hospital. Interested general practitioners should apply to Dr. S. W. HARDWICK, Royal Free Hospital, Gray's Inn Road, London, W.C.1.

Wessex Rahere Club.—Spring dinner, White Hart Hotel, Salisbury, April 30. Details will be circulated to members and to any other Barts men who are interested and who will get in touch with the honorary secretary, Mr. A. DAUNT BATEMAN, 11, The Circus, Bath.

St. Mary's Hospital Medical School Obstetrical and Gynaecological Conferences.—April–June, Tuesdays at 5 p.m., lecture theatre, Wright Fleming Institute. See *B.M.J.* diary each week for details.

10th Middle East Medical Assembly.—American University of Beirut, May 6–8. Details from Dr. R. E. NASSIF, Middle East Medical Assembly, American University of Beirut, Beirut, Lebanon.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 21

GROUP FOR REPRESENTATION OF THE VIEWS OF CLINICAL PSYCHIATRISTS.—At Rygate Room, Tavistock House North (Fourth Floor), Tavistock Square, W.C., 5.30 p.m., meeting.

●HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., dinner; 8.30 p.m., discussion to be opened by Air Commodore W. K. Stewart and Squadron Leader Peter Howard: Medical Hazards of Space Travel.

MANCHESTER MEDICAL SOCIETY: SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 4.30 for 5 p.m., Professor A. I. Darling: Early Attack of Caries.

Tuesday, March 22

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. M. Feiwel: Hirsutism.

LEEDS NEUROLOGICAL SCIENCES COLLOQUIUM, 1959-1960.—At Littlewood Hall, General Infirmary at Leeds, 5.15 p.m., Dr. Honor Smith: Intrathecal Tuberculin in Disseminated Sclerosis.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University Medical School, 4 for 4.30 p.m., University Lecture on the History of Medicine by Sir Gordon Gordon-Taylor: The Long Liston and the Fergusson Speculum.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor Sheila Sherlock.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arris and Gale Lecture by Mr. J. H. Peacock: Endocrine and Metabolic Aspects of Peripheral Blood Flow and Vasospastic Disease.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. N. G. Hulbert: Neurology.

Wednesday, March 23

EUGENICS SOCIETY.—At Rooms of Royal Society, Burlington House, Piccadilly, W., 5.30 p.m., Professor J. F. Danielli, F.R.S.: New Life in Old Bodies.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Immunological Aspects of Fungous Disease.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Pepys: Classification and Treatment of Asthma.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Calculi—Surgery.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University Medical School, 4 for 4.30 p.m., Professor P. R. Allison: Observations of the Pulmonary Circulation in Medical and Surgical Practice.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor H. Eddey: Surgery in Cancer of the Mouth.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. G. C. Snowie: Workwear for British Industry (illustrated).

Thursday, March 24

CHADWICK TRUST.—At Royal Society of Health, 5 p.m., Mr. D. A. Goldfinch: Hospital Sanitation.

LIVERPOOL MEDICAL INSTITUTION.—At Liverpool Dental Hospital, 2.30 p.m., afternoon clinical meeting.

NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, Oxford, 8.30 p.m., Dr. R. Nassim: Differential Diagnosis of the Porotic Spine.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson Demonstration by Dr. A. G. Stanfeld: Necrotizing Arteritis.

Friday, March 25

BIOCHEMICAL SOCIETY.—At School of Chemistry, University of Leeds, 10.30 a.m., 392nd meeting.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. C. Batten: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Mr. E. J. Radley Smith: Brain Abscess.

INSTITUTE OF PSYCHIATRY.—5.30 p.m., public lecture by Dr. G. K. Stürup (Copenhagen): Treatment of Criminal Psychopaths.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—At 11, Chandos Street, W., 7.30 p.m., general meeting. Dr. R. R. Willcox: Gonorrhoea and Infectious Venereal Disease in Great Britain. The Findings of Two Surveys Undertaken by the British Co-operative Clinical Group.

Saturday, March 26

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Department of Human Ecology, Fenner's, Gresham Road, Cambridge, Symposium on General Practice. *Morning*, 10.30 a.m., Dr. J. D. J. Havard (Assistant Secretary, B.M.A.): Relation of Alcohol to Road Accidents; 11.15 a.m., Dr. F. E. Camps: Medico-Legal Inquiries in General Practice; 11.55 a.m., Dr. R. I. Milne: Family Doctor and the Coroner; 12.35 p.m., questions and discussion. *Afternoon*, 2.30 p.m., film: Inquiry into General Practice, followed by general discussion opened by Dr. Bruce Cardew: "The Medical World."

APPOINTMENTS

BIRMINGHAM REGIONAL HOSPITAL BOARD.—**P. Griffiths**, M.B., B.Ch., D.O., Part-time Consultant Ophthalmologist to Burton-on-Trent Group of Hospitals; **A. I. Roith**, L.R.C.P.&S.I., D.C.H., D.P.M., Whole-time Consultant Psychiatrist and Deputy Medical Superintendent to Monyhull Hall; **P. C. Cashmore**, M.B., B.S., Whole-time Senior Casualty Officer (S.H.M.O.) to Burton-on-Trent Group of Hospitals.

GALLOWAY, T. McL., F.R.C.P.Ed., D.P.H., County Medical Officer of Health and Principal School Medical Officer, West Sussex, from April 1, 1960.

MANCHESTER REGIONAL HOSPITAL BOARD.—**L. T. Scott**, B.M., B.Ch., F.F.A. R.C.S., Maximum Part-time Consultant Anaesthetist, Lancaster and Kendal and Lancaster Moor Groups of Hospitals; **R. R. W. Hill**, M.B., B.S., F.F.A. R.C.S., Maximum Part-time Consultant Anaesthetist, Stockport and Buxton Group of Hospitals; **P. B. Woolley**, M.B., Ch.B., M.R.C.P., Maximum Part-time Consultant Chest Physician, Oldham and Ashton Hospital Centres; **K. S. Holmes**, M.B., Ch.B., F.F.R., D.M.R.T., D.Obst.R.C.O.G., Whole-time Assistant Radiotherapist (S.H.M.O.); **G. Garrett**, M.D., D.Path., Whole-time Consultant Pathologist, Oldham and District Group of Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Palfrey.—On February 28, 1960, to Ann (formerly Hewetson) and John Palfrey, a brother for Michael, Susan, and Christopher—David Keith.

DEATHS

Barford.—On February 23, 1960, at "Home," Bridgeway, Selsey, Sussex, Percy Crompe Barford, M.B., aged 91.

Birkett.—On February 21, 1960, at 2, Highbury Hall, Weston-super-Mare, Som., Jane Louisa Jarrett Birkett, M.D., aged 94.

Bree.—On February 23, 1960, at "Rozel," Felpham, Sussex, Sidney Bree, M.B., formerly of Manningtree, Essex, aged 83.

Briggs.—On March 3, 1960, at Eastbourne, Sussex, Norman Briggs, C.I.E., M.R.C.S., L.R.C.P., D.P.H., colonel, I.M.S., retired, aged 68.

Bulman.—On February 17, 1960, in hospital, John Roderick Bulman, M.B., Ch.B., of 20, Aylestone Hill, Hereford, aged 74.

Dunn.—On February 21, 1960, in hospital, Alexander Finlayson Dunn, T.D., M.B., Ch.B., of 4, Christchurch Road, Folkestone, Kent, aged 59.

Jones.—On February 21, 1960, at Worthing Hospital, John Christopher Jones, M.B., Ch.B., of 107, Grand Avenue, Worthing, Sussex, late of South Norwood, London, S.E., aged 71.

Kibble.—On February 21, 1960, at Ridgemead House, Englefield Green, Surrey, Caroline Baxter Kibble, M.B.E., M.R.C.S., L.R.C.P., late of Malaya.

Lawrence.—On February 23, 1960, William Jamieson Lawrence, M.B., Ch.B., of 29, Thurloe Place, London, S.W.

Pinkerton.—On February 20, 1960, Samuel Pinkerton, M.B., F.R.C.S.Ed., of 10, Cornwall Road, Stroud Green, London, N., and 11, South Gray Street, Edinburgh.

Valdez.—On February 19, 1960, Frederick Augustine Valdez, M.B., B.Ch., of 3, North Road, Longsight, Manchester.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Coronary Arterial Spasm

Q.—*Is there such a thing as coronary arterial spasm? How can it be diagnosed and treated?*

A.—Patients with recurrent and typical cardiac pain on effort or at rest for many years, associated with a good prognosis, have been diagnosed as having coronary arterial spasm. The cardiogram in these patients showed minor changes in the S-T T wave, or marked and widespread inversion of the T wave which reverted to normal after an interval. The pain and acute cardiographic changes were considered to be due to cardiac ischaemia resulting from spasm of the left coronary artery distal to the circumflex branch and proximal to the left marginal branch, the artery being unaffected by occlusive sclerosis.[1]

However, spasm of the coronary arteries is not commonly considered to be of clinical significance. The pain in patients credited with this condition is usually either angina pectoris due to coronary artery disease or is not of cardiac origin. When the pain is true angina, the patient should usually be regarded as having ischaemic heart disease and treated accordingly unless there is evidence of an obstructive cardiac lesion (such as aortic or pulmonary stenosis), coronary embolism, or cardiomyopathy. Severe anaemia may be associated with true angina, which then disappears when the anaemia is corrected, but there is no evidence that the pain is due to coronary arterial spasm. Likewise, angina in thyrotoxicosis may resolve with antithyroid treatment, but is regarded as being due to associated ischaemic heart disease.[2]

Any patient thought to be suffering from coronary arterial spasm should be carefully investigated for evidence of organic disease of the heart or elsewhere, while great care should be taken to avoid an erroneous diagnosis of angina in patients with benign chest pain of skeletal origin, or with anxiety neurosis.

REFERENCES

1 Evans, W., *Brit. Heart J.*, 1955, **17**, 15.
2 Sandler, G., and Wilson, G. M., *Quart. J. Med.*, 1959, **28**, 347.

Routine Radioscopy and Lung Cancer

Q.—*Might repeated x-ray examination of the chest be a factor in causing lung cancer? Should it be taken into account in making routine radioscopy of chest compulsory for factory workers, Service personnel, candidates for life assurance, etc.?*

A.—There is no evidence whatever that repeated *x*-ray examinations of the chest are a factor in the causation of lung cancer. For over thirty years extensive repeat chest *x*-ray examinations were made for the control of tuberculosis, and for a very long period of time the number of tuberculous patients on the register was in the neighbourhood of 400,000. It is exceptional to find tuberculosis and cancer of the lung together, and the many chest physicians involved in the control of tuberculosis would have noted any increased incidence of lung cancer in their patients.

Psychological Factors in Hypertension

Q.—*What is the importance of psychological factors in the aetiology of hypertension, and can hypertension so caused become permanent and lead to the common complications?*

A.—Genetic factors account for only a part of the variations about the mean of blood-pressure at any age. Thus the degree of resemblance amongst siblings for height is expressed by a coefficient of 0.5, whereas that for blood-pressure has a co-efficient of a little over 0.2. Clearly, then, environmental factors must be important in determining the actual level of blood-pressure, including the values termed hypertension. What these environmental factors are is as yet uncertain, but it is quite likely that psychological factors are important. Their exact nature has not been defined.

It is known that the blood-pressure may remain unaltered when the apparent cause of hypertension is removed. It seems not unlikely that if psychological factors lead to long-continued elevation of blood-pressure this may in time become permanent. The common complications of raised blood-pressure occur in every type of prolonged hypertension, whether secondary or so-called essential hypertension. It therefore seems not unlikely that if psychological factors are concerned in the aetiology of hypertension this type of hypertension may lead to the common complications of the disease.

Sensitivity to Sulphonamides

Q.—*(1) Is a patient sensitive to sulphamezathine likely to be sensitive to other sulphonamides? (2) Is it possible to desensitize a patient who had a mild anaphylactic reaction after a single dose of a triple sulphonamide preparation?*

A.—Readministration of any sulphonamide to a patient who has previously had an anaphylactic reaction from drugs of this group may result in a recurrence or more serious reactions. Sensitization may last for several years and effective desensitization procedures are unknown.

Blood-stained Colostrum

Q.—*A healthy woman aged 21 is now five months pregnant and the secretion from both breasts has been stained with blood for three months. There are no physical signs and she has had no hormone treatment or local massage. Is there any significance in this?*

A.—Slight staining of colostrum with blood does sometimes occur without an apparent organic basis. The phenomenon may affect either one or both breasts and may recur with each pregnancy. When it is bilateral, as in this case, it is least likely to be caused by a local lesion such as a duct papilloma. In the absence of any apparent abnormality in the breast, the occurrence is thought to be related to the increased vascularity associated with pregnancy. It is to be regarded as having no serious significance, and it should disappear spontaneously when pregnancy and lactation are complete. If it does not, the situation should then be reviewed.

Correction.—We regret that "prostigmin" was not distinguished as a proprietary name in the *Journal* of February 27, page 640.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Refresher Course for General Practitioners, Volume 3 (26s. 9d.).

Clinical Pathology in General Practice (22s. 3d.).

Any Questions?, Volume 3 (8s. 3d.).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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